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(57) Abstract

Methods for treating conditions or disorders which can be alleviated by reducing food intake are disclosed which comprise administration of an effective amount of an exendin or an exendin agonist, alone or in conjunction with other compounds or compositions that effect satiety. The methods are useful for treating conditions or disorders, including obesity, Type II diabetes, eating disorders, and insulin–resistance syndrome. The methods are also useful for lowering the plasma glucose level, lowering the plasma lipid level, reducing the cardiac risk, reducing the appetite, and reducing the weight of subjects. Pharmaceutical compositions for use in the methods of the invention are also disclosed.

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USE OF EXENDINS AND AGONISTS THEREOF FOR THE REDUCTION OF FOOD INTAKE

This application claims the benefit of U.S. Provisional Application No. 60/034,905, filed January 7, 1997, U.S. Provisional Application No. 60/055,404, filed August 8, 1997, U.S. Provisional Application No. 60/066,029 filed November 14, 1997, and U.S. Provisional Application No. 60/065,442, November 14, 1997.

FIELD OF THE INVENTION

The present invention relates to methods for treating conditions or disorders which can be alleviated by reducing food intake comprising administration of an effective amount of an exendin or an exendin agonist alone or in conjunction with other compounds or compositions that affect satiety such as a leptin or an amylin agonist. The methods are useful for treating conditions or disorders, in which the reduction of food intake is of value, including obesity, Type II diabetes, eating disorders, and insulin-resistance syndrome. The methods are also useful for lowering the plasma lipid level, reducing the cardiac risk, reducing the appetite, and reducing the weight of subjects. Pharmaceutical compositions for use in the methods of the invention are also disclosed.

BACKGROUND

The following description summarizes information relevant to the present invention. It is not an admission that any of the information provided herein is prior art to the presently claimed invention, nor that any of the publications specifically or implicitly referenced are prior art to that invention.

Exendin

Exendins are peptides that are found in the venom of the Gila-monster, a lizard found in Arizona, and the Mexican Beaded Lizard. Exendin-3 is present in the venom of Heloderma horridum, and exendin-4 is present in the venom of Heloderma suspectum (Eng, J., et al., J. Biol. Chem., 265:20259-62, 1990; Eng., J., et al., J. Biol. Chem., 267:7402-05, 1992). The exendins have some sequence similarity to several members of the glucagon-like peptide family, with the highest homology, 53%, being to GLP-1[7-36]NH_2 (Goke, et al., J. Biol. Chem., 268:19650-55, 1993). GLP-1[7-36]NH_2, also known as proglucagon[78-107], has an insulinotropic effect, stimulating insulin secretion from pancreatic β-cells; GLP also inhibits glucagon secretion from pancreatic α-cells (Orskov, et al., Diabetes, 42:658-61, 1993; D'Alessio, et al., J. Clin. Invest., 97:133-38, 1996). GLP-1 is reported to inhibit gastric emptying (Williams B, et al., J Clin Endocrinol Metab 81 (1): 327-32, 1996; Wettergren A, et al., Dig Dis Sci 38 (4): 665-73, 1993), and gastric acid

secretion. (Schjoldager BT, et al., Dig Dis Sci 34 (5): 703-8, 1989; O'Halloran DJ, et al., J Endocrinol 126 (1): 169-73, 1990; Wettergren A, et al., Dig Dis Sci 38 (4): 665-73, 1993). GLP-1[7-37], which has an additional glycine residue at its carboxy terminus, also stimulates insulin secretion in humans (Orskov, et al., Diabetes, 42:658-61, 1993). A transmembrane G-protein adenylate-cyclase-coupled receptor believed to be responsible for the insulinotropic effect of GLP-1 is reported to have been cloned from a β-cell line (Thorens, Proc. Natl. Acad. Sci. USA 89:8641-45 (1992)).

Exendin-4 potently binds at GLP-1 receptors on insulin-secreting βTC1 cells, at dispersed acinar cells from guinea pig pancreas, and at parietal cells from stomach; the peptide is also said to stimulate somatostatin release and inhibit gastrin release in isolated stomachs (Goke, et al., J. Biol. Chem. 268:19650-55, 1993; Schepp, et al., Eur. J. Pharmacol., 69:183-91, 1994; Eissele, et al., Life Sci., 55:629-34, 1994). Exendin-3 and exendin-4 were reported to stimulate cAMP production in, and amylase release from, pancreatic acinar cells (Malhotra, R., et al., Regulatory Peptides,41:149-56, 1992; Raufman, et al., J. Biol. Chem. 267:21432-37, 1992; Singh, et al., Regul. Pept. 53:47-59, 1994). The use of exendin-3 and exendin-4 as insulinotrophic agents for the treatment of diabetes mellitus and the prevention of hyperglycemia has been proposed (Eng, U.S. Patent No. 5,424,286).

C-terminally truncated exendin peptides such as exendin[9-39], a carboxyamidated molecule, and fragments 3-39 through 9-39 have been reported to be potent and selective antagonists of GLP-1 (Goke, et al., J. Biol. Chem., 268:19650-55, 1993; Raufman, J.P., et al., J. Biol. Chem. 266:2897-902, 1991; Schepp, W., et al., Eur. J. Pharm. 269:183-91, 1994; Montrose-Rafizadeh, et al., Diabetes, 45(Suppl. 2):152A, 1996). Exendin[9-39] is said to block endogenous GLP-1 in vivo, resulting in reduced insulin secretion. Wang, et al., J. Clin. Invest., 95:417-21, 1995; D'Alessio, et al., J. Clin. Invest., 97:133-38, 1996). The receptor apparently responsible for the insulinotropic effect of GLP-1 has reportedly been cloned from rat pancreatic islet cell (Thorens, B., Proc. Natl. Acad. Sci. USA 89:8641-8645, 1992). Exendins and exendin[9-39] are said to bind to the cloned GLP-1 receptor (rat pancreatic β-cell GLP-1 receptor (Fehmann HC, et al., Peptides 15 (3): 453-6, 1994) and human GLP-1 receptor (Thorens B, et al., Diabetes 42 (11): 1678-82, 1993). In cells transfected with the cloned GLP-1 receptor, exendin-4 is reportedly an agonist, i.e., it increases cAMP, while exendin[9-39] is identified as an antagonist, i.e., it blocks the stimulatory actions of exendin-4 and GLP-1. Id.

Exendin[9-39] is also reported to act as an antagonist of the full length exendins, inhibiting stimulation of pancreatic acinar cells by exendin-3 and exendin-4 (Raufman, et al., J. Biol. Chem. 266:2897-902,

1991; Raufman, et al., J. Biol. Chem., 266:21432-37, 1992). It is also reported that exendin[9-39] inhibits the stimulation of plasma insulin levels by exendin-4, and inhibits the somatostatin release-stimulating and gastrin release-inhibiting activities of exendin-4 and GLP-1 (Kolligs, F., et al., Diabetes, 44:16-19, 1995; Eissele, et al., Life Sciences, 55:629-34, 1994).

Exendins have recently been found to inhibit gastric emptying (U.S.S.N. 08/694,954, filed August 8, 1996, which enjoys common ownership with the present invention and is hereby incorporated by reference).

Exendin [9-39] has been used to investigate the physiological relevance of central GLP-1 in control of food intake (Turton, M.D. et al. Nature 379:69-72, 1996). GLP-1 administered by intracerebroventricular injection inhibits food intake in rats. This satiety-inducing effect of GLP-1 delivered ICV is reported to be inhibited by ICV injection of exendin [9-39] (Turton, supra). However, it has been reported that GLP-1 does not inhibit food intake in mice when administered by peripheral injection (Turton, M.D., Nature 379:69-72, 1996; Bhavsar, S.P., Soc. Neurosci. Abstr. 21:460 (188.8), 1995).

Obesity and Hypernutrition

Obesity, excess adipose tissue, is becoming increasingly prevalent in developed societies. For example, approximately 30% of adults in the U.S. were estimated to be 20 percent above desirable body weight -- an accepted measure of obesity sufficient to impact a health risk (*Harrison's Principles of Internal Medicine*

12th Edition, McGraw Hill, Inc. (1991) p. 411). The pathogenesis of obesity is believed to be multifactorial but the basic problem is that in obese subjects food intake and energy expenditure do not come into balance until there is excess adipose tissue. Attempts to reduce food intake, or hypernutrition, are usually fruitless in the medium term because the weight loss induced by dieting results in both increased appetite and decreased energy expenditure (Leibel et al., (1995) *New England Journal of Medicine* 322: 621-628). The intensity of physical exercise required to expend enough energy to materially lose adipose mass is too great for most people to undertake on a sufficiently frequent basis. Thus, obesity is currently a poorly treatable, chronic, essentially intractable metabolic disorder. Not only is obesity itself believed by some to be undesirable for cosmetic reasons, but obesity also carries serious risk of co-morbidities including, Type 2 diabetes, increased cardiac risk, hypertension, atherosclerosis, degenerative arthritis, and increased incidence of complications of surgery involving general anesthesia. Obesity due to hypernutrition is also a risk factor for the group of conditions called insulin resistance syndrome, or "syndrome X." In syndrome X, it has been reported that there is a linkage between insulin resistance and hypertension. (Watson N. and Sandler M., *Curr. Med. Res. Opin.*, 12(6):374-378 (1991); Kodama J. et al., *Diabetes Care*, 13(11):1109-1111 (1990); Lithell et al., *J. Cardiovasc. Pharmacol.*, 15 Suppl. 5:S46-S52 (1990)).

In those few subjects who do succeed in losing weight, by about 10 percent of body weight, there can be striking improvements in co-morbid conditions, most especially Type 2 diabetes in which dieting and weight loss are the primary therapeutic modality, albeit relatively ineffective in many patients for the reasons stated above. Reducing food intake in obese subjects would decrease the plasma glucose level, the plasma lipid level, and the cardiac risk in these subjects. Hypernutrition is also the result of, and the psychological cause of, many eating disorders. Reducing food intake would also be beneficial in the treatment of such disorders.

Thus, it can be appreciated that an effective means to reduce food intake is a major challenge and a superior method of treatment would be of great utility. Such a method, and compounds and compositions which are useful therefor, have been invented and are described and claimed herein.

SUMMARY OF THE INVENTION

The present invention concerns the surprising discovery that exendins and exendin agonists have a profound and prolonged effect on inhibiting food intake.

The present invention is directed to novel methods for treating conditions or disorders associated with hypernutrition, comprising the administration of an exendin, for example, exendin-3 [SEQ ID NO. 1: His Ser Asp

Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro Ser], or exendin-4 [SEQ ID NO. 2: His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro Ser], or other compounds which effectively bind to the receptor at which exendin exerts its action on reducing food intake. These methods will be useful in the treatment of, for example, obesity, diabetes, including Type II or non-insulin dependent diabetes, eating disorders, and insulin-resistance syndrome.

In a first aspect, the invention features a method of treating conditions or disorders which can be alleviated by reducing food intake in a subject comprising administering to the subject a therapeutically effective amount of an exendin or an exendin agonist. By an "exendin agonist" is meant a compound that mimics the effects of exendin on the reduction of food intake by binding to the receptor or receptors where exendin causes this effect. Preferred exendin agonist compounds include those described in United States Provisional Patent Application Serial No. 60/055,404, entitled, "Novel Exendin Agonist Compounds," filed August 8, 1997; United States Provisional Patent Application Serial No. 60/065,442, entitled, "Novel Exendin Agonist Compounds," filed November 14, 1997; and United States Provisional Patent Application Serial No. 60/066,029, entitled, "Novel Exendin Agonist Compounds," filed November 14, 1997; all of which enjoy common

ownership with the present application and all of which are incorporated by this reference into the present application as though fully set forth herein. By "condition or disorder which can be alleviated by reducing food intake" is meant any condition or disorder in a subject that is either caused by, complicated by, or aggravated by a relatively high food intake, or that can be alleviated by reducing food intake. Such conditions or disorders include, but are not limited to, obesity, diabetes, including Type II diabetes, eating disorders, and insulin-resistance syndrome.

Thus, in a first embodiment, the present invention provides a method for treating conditions or disorders which can be alleviated by reducing food intake in a subject comprising administering to said subject a therapeutically effective amount of an exendin or an exendin agonist. Preferred exendin agonist compounds include those described in U.S. Provisional Patent Application Serial Nos. 60/055,404; 60/065,442; and 60/066,029, which have been incorporated by reference in the present application. Preferably, the subject is a vertebrate, more preferably a mammal, and most preferably a human. In preferred aspects, the exendin or exendin agonist is administered parenterally, more preferably by injection. In a most preferred aspect, the injection is a peripheral injection. Preferably, about 10 μg-30 μg to about 5 mg of the exendin or exendin agonist is administered per day. More preferably, about 10-30 μg to about 2mg, or about 10-30 μg to about 1mg of the exendin or

exendin agonist is administered per day. Most preferably, about 30 μg to about 500 μg of the exendin or exendin agonist is administered per day.

In various preferred embodiments of the invention, the condition or disorder is obesity, diabetes, preferably Type II diabetes, an eating disorder, or insulin-resistance syndrome.

In other preferred aspects of the invention, a method is provided for reducing the appetite of a subject comprising administering to said subject an appetite-lowering amount of an exendin or an exendin agonist.

In yet other preferred aspects, a method is provided for lowering plasma lipids comprising administering to said subject a therapeutically effective amount of an exendin or an exendin agonist.

The methods of the present invention may also be used to reduce the cardiac risk of a subject comprising administering to said subject a therapeutically effective amount of an exendin or an exendin agonist. In one preferred aspect, the exendin or exendin agonist used in the methods of the present invention is exendin-3. In another preferred aspect, said exendin is exendin-4. Other preferred exendin agonists include exendin-4 (1-30) [SEQ ID NO 6: His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly], exendin-4 (1-30) amide [SEQ ID NO 7: His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly-NH_2], exendin-4 (1-28) amide [SEQ ID NO 40: His Gly Glu Gly Thr

Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2], ^{14}Leu,^{25}Phe exendin-4 amide [SEQ ID NO 9: His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro Ser-NH_2], ^{14}Leu,^{25}Phe exendin-4 (1-28) amide [SEQ ID NO 41: His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2], and ^{14}Leu,^{22}Ala,^{25}Phe exendin-4 (1-28) amide [SEQ ID NO 8: His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Ala Ile Glu Phe Leu Lys Asn-NH_2].

In the methods of the present invention, the exendins and exendin agonists may be administered separately or together with one or more other compounds and compositions that exhibit a long term or short-term satiety action, including, but not limited to other compounds and compositions that comprise an amylin agonist, cholecystokinin (CCK), or a leptin (ob protein). Suitable amylin agonists include, for example, [^{25,28,29}Pro-]-human amylin (also known as "pramlintide," and previously referred to as "AC-137") as described in "Amylin Agonist Peptides and Uses Therefor," U.S. Patent No. 5,686,511, issued November 11, 1997, and salmon calcitonin. The CCK used is preferably CCK octopeptide (CCK-8). Leptin is discussed in, for example, Pelleymounter, M.A., et al. Science 269:540-43 (1995); Halaas, J.L., et al. Science 269:543-46 (1995); and Campfield, L.A., et al. Eur. J. Pharmac. 262:133-41 (1994).

In other embodiments of the invention is provided a pharmaceutical composition for use in the treatment of conditions or disorders which can be alleviated by reducing food intake comprising a therapeutically effective amount of an exendin or exendin agonist in association with a pharmaceutically acceptable carrier. Preferably, the pharmaceutical composition comprises a therapeutically effective amount for a human subject.

The pharmaceutical composition may preferably be used for reducing the appetite of a subject, reducing the weight of a subject, lowering the plasma lipid level of a subject, or reducing the cardiac risk of a subject. Those of skill in the art will recognize that the pharmaceutical composition will preferably comprise a therapeutically effective amount of an exendin or exendin agonist to accomplish the desired effect in the subject.

The pharmaceutical compositions may further comprise one or more other compounds and compositions that exhibit a long-term or short-term satiety action, including, but not limited to other compounds and compositions that comprise an amylin agonist, CCK, preferably CCK-8, or leptin. Suitable amylin agonists include, for example, [^{25,28,29}Pro]-human amylin and salmon calcitonin.

In one preferred aspect, the pharmaceutical composition comprises exendin-3. In another preferred aspect, the pharmaceutical composition comprises exendin-4. In other preferred aspects, the pharmaceutical compositions comprises a peptide selected from: exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28) amide,

^{14}Leu,^{25}Phe exendin-4 amide, ^{14}Leu,^{25}Phe exendin-4 (1-28) amide, and ^{14}Leu,^{22}Ala,^{25}Phe exendin-4 (1-28) amide.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a graphical depiction of the change of food intake in normal mice after intraperitoneal injection of exendin-4 and GLP-1.

Figure 2 is a graphical depiction of the change of food intake in obese mice after intraperitoneal injection of exendin-4.

Figure 3 is a graphical depiction of the change of food intake in rats after intracerebroventricular injection of exendin-4

Figure 4 is a graphical depiction of the change of food intake in normal mice after intraperitoneal injection of exendin-4 (1-30) ("Compound 1").

Figure 5 is a graphical depiction of the change of food intake in normal mice after intraperitoneal injection of exendin-4 (1-30) amide ("Compound 2").

Figure 6 is a graphical depiction of the change of food intake in normal mice after intraperitoneal injection of exendin-4 (1-28) amide ("Compound 3").

Figure 7 is a graphical depiction of the change of food intake in normal mice after intraperitoneal injection of ^{14}Leu,^{25}Phe exendin-4 amide ("Compound 4").

Figure 8 is a graphical depiction of the change of food intake in normal mice after intraperitoneal injection of ^{14}Leu,^{25}Phe exendin-4 (1-28) amide ("Compound 5").

Figure 9 is a graphical depiction of the change of food intake in normal mice after intraperitoneal injection of ^{14}Leu,^{22}Ala,^{25}Phe exendin-4 (1-28) amide ("Compound 6").

Figure 10 depicts the amino acid sequences for certain exendin agonist compounds useful in the present invention [SEQ ID NOS 9-39].

DETAILED DESCRIPTION OF THE INVENTION

Exendins and exendin agonists are useful as described herein in view of their pharmacological properties. Activity as exendin agonists can be indicated by activity in the assays described below. Effects of exendins or exendin agonists on reducing food intake can be identified, evaluated, or screened for, using the methods described in the Examples below, or other methods known in the art for determining effects on food intake or appetite.

Exendin Agonist Compounds

Exendin agonist compounds are those described in U.S. Provisional Application No. 60/055,404, including compounds of the formula (I) [SEQ ID NO. 3]:

```
1                        5                       10
Xaa1 Xaa2 Xaa3 Gly Thr Xaa4 Xaa5 Xaa6 Xaa7 Xaa8
                    15                      20
Ser Lys Gln Xaa9 Glu Glu Glu Ala Val Arg Leu
                  25                        30
Xaa10 Xaa11 Xaa12 Xaa13 Leu Lys Asn Gly Gly Xaa14
            35
Ser Ser Gly Ala Xaa15 Xaa16 Xaa17 Xaa18-Z
```

wherein Xaa_1 is His, Arg or Tyr; Xaa_2 is Ser, Gly, Ala or Thr; Xaa_3 is Asp or Glu; Xaa_4 is Phe, Tyr or naphthylalanine; Xaa_5 is Thr or Ser; Xaa_6 is Ser or Thr; Xaa_7 is Asp or Glu; Xaa_8 is Leu, Ile, Val, pentylglycine or Met; Xaa_9 is Leu, Ile, pentylglycine, Val or Met; Xaa_{10} is Phe, Tyr or naphthylalanine; Xaa_{11} is Ile, Val, Leu, pentylglycine, tert-butylglycine or Met; Xaa_{12} is Glu or Asp; Xaa_{13} is Trp, Phe, Tyr, or naphthylalanine; Xaa_{14}, Xaa_{15}, Xaa_{16} and Xaa_{17} are independently Pro, homoproline, 3Hyp, 4Hyp, thioproline, N-alkylglycine, N-alkylpentylglycine or N-alkylalanine; Xaa_{18} is Ser, Thr or Tyr; and Z is -OH or $-NH_2$; with the proviso that the compound is not exendin-3 or exindin-4.

Preferred N-alkyl groups for N-alkylglycine, N-alkylpentylglycine and N-alkylalanine include lower alkyl groups preferably of 1 to about 6 carbon atoms, more preferably of 1 to 4 carbon atoms. Suitable compounds include those listed in Figure 10 having amino acid sequences of SEQ. ID. NOS. 9 to 39.

Preferred exendin agonist compounds include those wherein Xaa_1 is His or Tyr. More preferably Xaa_1 is His.

Preferred are those compounds wherein Xaa_2 is Gly.

Preferred are those compounds wherein Xaa_9 is Leu, pentylglycine or Met.

Preferred compounds include those wherein Xaa_{13} is Trp or Phe.

Also preferred are compounds where Xaa_4 is Phe or naphthylalanine; Xaa_{11} is Ile or Val and Xaa_{14}, Xaa_{15}, Xaa_{16}

and Xaa_{17} are independently selected from Pro, homoproline, thioproline or N-alkylalanine. Preferably N-alkylalanine has a N-alkyl group of 1 to about 6 carbon atoms.

According to an especially preferred aspect, Xaa_{15}, Xaa_{16} and Xaa_{17} are the same amino acid reside.

Preferred are compounds wherein Xaa_{18} is Ser or Tyr, more preferably Ser.

Preferably Z is $-NH_2$.

According to one aspect, preferred are compounds of formula (I) wherein Xaa_1 is His or Tyr, more preferably His; Xaa_2 is Gly; Xaa_4 is Phe or naphthylalanine; Xaa_9 is Leu, pentylglycine or Met; Xaa_{10} is Phe or naphthylalanine; Xaa_{11} is Ile or Val; Xaa_{14}, Xaa_{15}, Xaa_{16} and Xaa_{17} are independently selected from Pro, homoproline, thioproline or N-alkylalanine; and Xaa_{18} is Ser or Tyr, more preferably Ser. More preferably Z is $-NH_2$.

According to an especially preferred aspect, especially preferred compounds include those of formula (I) wherein: Xaa_1 is His or Arg; Xaa_2 is Gly; Xaa_3 is Asp or Glu; Xaa_4 is Phe or napthylalanine; Xaa_5 is Thr or Ser; Xaa_6 is Ser or Thr; Xaa_7 is Asp or Glu; Xaa_8 is Leu or pentylglycine; Xaa_9 is Leu or pentylglycine; Xaa_{10} is Phe or naphthylalanine; Xaa_{11} is Ile, Val or t-butyltylglycine; Xaa_{12} is Glu or Asp; Xaa_{13} is Trp or Phe; Xaa_{14}, Xaa_{15}, Xaa_{16}, and Xaa_{17} are independently Pro, homoproline, thioproline, or N-methylalanine; Xaa_{18} is Ser or Tyr: and Z is -OH or $-NH_2$; with the proviso that the compound does not have the formula of either SEQ. ID. NOS. 1 or 2. More preferably Z

is $-NH_2$. Especially preferred compounds include those having the amino acid sequence of SEQ. ID. NOS. 9, 10, 21, 22, 23, 26, 28, 34, 35 and 39.

According to an especially preferred aspect, provided are compounds where Xaa_9 is Leu, Ile, Val or pentylglycine, more preferably Leu or pentylglycine, and Xaa_{13} is Phe, Tyr or naphthylalanine, more preferably Phe or naphthylalanine. These compounds will exhibit advantageous duration of action and be less subject to oxidative degration, both in vitro and in vivo, as well as during synthesis of the compound.

Exendin agonist compounds also include those described in U.S. Provisional Application No. 60/065,442, including compounds of the formula (II) [SEQ ID NO. 4]:

$Xaa_1\ Xaa_2\ Xaa_3\ Gly\ Xaa_5\ Xaa_6\ Xaa_7\ Xaa_8\ Xaa_9\ Xaa_{10}$
$Xaa_{11}\ Xaa_{12}\ Xaa_{13}\ Xaa_{14}\ Xaa_{15}\ Xaa_{16}\ Xaa_{17}\ Ala\ Xaa_{19}\ Xaa_{20}$
$Xaa_{21}\ Xaa_{22}\ Xaa_{23}\ Xaa_{24}\ Xaa_{25}\ Xaa_{26}\ Xaa_{27}\ Xaa_{28}-Z_1$; wherein

Xaa_1 is His, Arg or Tyr;
Xaa_2 is Ser, Gly, Ala or Thr;
Xaa_3 is Asp or Glu;
Xaa_5 is Ala or Thr;
Xaa_6 is Ala, Phe, Tyr or naphthylalanine;
Xaa_7 is Thr or Ser;
Xaa_8 is Ala, Ser or Thr;
Xaa_9 is Asp or Glu;

Xaa_{10} is Ala, Leu, Ile, Val, pentylglycine or Met;

Xaa_{11} is Ala or Ser;

Xaa_{12} is Ala or Lys;

Xaa_{13} is Ala or Gln;

Xaa_{14} is Ala, Leu, Ile, pentylglycine, Val or Met;

Xaa_{15} is Ala or Glu;

Xaa_{16} is Ala or Glu;

Xaa_{17} is Ala or Glu;

Xaa_{19} is Ala or Val;

Xaa_{20} is Ala or Arg;

Xaa_{21} is Ala or Leu;

Xaa_{22} is Ala, Phe, Tyr or naphthylalanine;

Xaa_{23} is Ile, Val, Leu, pentylglycine, tert-butylglycine or Met;

Xaa_{24} is Ala, Glu or Asp;

Xaa_{25} is Ala, Trp, Phe, Tyr or naphthylalanine;

Xaa_{26} is Ala or Leu;

Xaa_{27} is Ala or Lys;

Xaa_{28} is Ala or Asn;

Z_1 is -OH,

$-NH_2$

Gly-Z_2,

Gly Gly-Z_2,

Gly Gly Xaa_{31}-Z_2,

Gly Gly Xaa_{31} Ser-Z_2,

Gly Gly Xaa_{31} Ser Ser-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly Ala-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36}-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36} Xaa_{37}-Z_2 or

Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36} Xaa_{37} Xaa_{38}-Z_2;

Xaa_{31}, Xaa_{36}, Xaa_{37} and Xaa_{38} are independently Pro, homoproline, 3Hyp, 4Hyp, thioproline, N-alkylglycine, N-alkylpentylglycine or N-alkylalanine; and

Z_2 is -OH or $-NH_2$;

provided that no more than three of Xaa_3, Xaa_5, Xaa_6, Xaa_8, Xaa_{10}, Xaa_{11}, Xaa_{12}, Xaa_{13}, Xaa_{14}, Xaa_{15}, Xaa_{16}, Xaa_{17}, Xaa_{19}, Xaa_{20}, Xaa_{21}, Xaa_{24}, Xaa_{25}, Xaa_{26}, Xaa_{27} and Xaa_{28} are Ala. Preferred N-alkyl groups for N-alkylglycine, N-alkylpentylglycine and N-alkylalanine include lower alkyl groups preferably of 1 to about 6 carbon atoms, more preferably of 1 to 4 carbon atoms.

Preferred exendin agonist compounds include those wherein Xaa_1 is His or Tyr. More preferably Xaa_1 is His.

Preferred are those compounds wherein Xaa_2 is Gly.

Preferred are those compounds wherein Xaa_{14} is Leu, pentylglycine or Met.

Preferred compounds are those wherein Xaa_{25} is Trp or Phe.

Preferred compounds are those where Xaa_6 is Phe or naphthylalanine; Xaa_{22} is Phe or naphthylalanine and Xaa_{23} is Ile or Val.

Preferred are compounds wherein Xaa_{31}, Xaa_{36}, Xaa_{37} and Xaa_{38} are independently selected from Pro, homoproline, thioproline and N-alkylalanine.

Preferably Z_1 is $-NH_2$.

Preferable Z_2 is $-NH_2$.

According to one aspect, preferred are compounds of formula (I) wherein Xaa_1 is His or Tyr, more preferably His; Xaa_2 is Gly; Xaa_6 is Phe or naphthylalanine; Xaa_{14} is Leu, pentylglycine or Met; Xaa_{22} is Phe or naphthylalanine; Xaa_{23} is Ile or Val; Xaa_{31}, Xaa_{36}, Xaa_{37} and Xaa_{38} are independently selected from Pro, homoproline, thioproline or N-alkylalanine. More preferably Z_1 is $-NH_2$.

According to an especially preferred aspect, especially preferred compounds include those of formula (I) wherein: Xaa_1 is His or Arg; Xaa_2 is Gly or Ala; Xaa_3 is Asp or Glu; Xaa_5 is Ala or Thr; Xaa_6 is Ala, Phe or nephthylalaine; Xaa_7 is Thr or Ser; Xaa_8 is Ala, Ser or Thr; Xaa_9 is Asp or Glu; Xaa_{10} is Ala, Leu or pentylglycine; Xaa_{11} is Ala or Ser; Xaa_{12} is Ala or Lys; Xaa_{13} is Ala or Gln; Xaa_{14} is Ala, Leu or pentylglycine; Xaa_{15} is Ala or Glu; Xaa_{16} is Ala or Glu; Xaa_{17} is Ala or Glu; Xaa_{19} is Ala or Val; Xaa_{20} is Ala or Arg; Xaa_{21} is Ala or Leu; Xaa_{22} is Phe or naphthylalanine; Xaa_{23} is Ile, Val or tert-butylglycine; Xaa_{24} is Ala, Glu or Asp; Xaa_{25} is Ala, Trp or Phe; Xaa_{26} is Ala or Leu; Xaa_{27} is Ala or Lys; Xaa_{28} is Ala or Asn; Z_1 is -OH, $-NH_2$, Gly-Z_2, Gly Gly-Z_2, Gly Gly Xaa_{31}-Z_2, Gly Gly Xaa_{31} Ser-Z_2, Gly Gly Xaa_{31} Ser Ser-Z_2, Gly Gly Xaa_{31} Ser Ser Gly-Z_2, Gly Gly Xaa_{31} Ser Ser Gly Ala-Z_2, Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36}-Z_2, Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36} Xaa_{37}-Z_2, Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36} Xaa_{37} Xaa_{38}-Z_2; Xaa_{31}, Xaa_{36}, Xaa_{37} and Xaa_{38} being independently Pro homoproline, thioproline or N-

methylalanine; and Z_2 being -OH or $-NH_2$; provided that no more than three of Xaa_3, Xaa_5, Xaa_6, Xaa_8, Xaa_{10}, Xaa_{11}, Xaa_{12}, Xaa_{13}, Xaa_{14}, Xaa_{15}, Xaa_{16}, Xaa_{17}, Xaa_{19}, Xaa_{20}, Xaa_{21}, Xaa_{24}, Xaa_{25}, Xaa_{26}, Xaa_{27} and Xaa_{28} are Ala. Especially preferred compounds include those having the amino acid sequence of SEQ. ID. NOS. 40-61.

According to an especially preferred aspect, provided are compounds where Xaa_{14} is Leu, Ile, Val or pentylglycine, more preferably Leu or pentylglycine, and Xaa_{25} is Phe, Tyr or naphthylalanine, more preferably Phe or naphthylalanine. These compounds will be less susceptive to oxidative degration, both in vitro and in vivo, as well as during synthesis of the compound.

Exendin agonist compounds also include those described in U.S. Provisional Application No. 60/066,029, including compounds of the formula (III)[SEQ ID NO. 5]:

Xaa_1 Xaa_2 Xaa_3 Xaa_4 Xaa_5 Xaa_6 Xaa_7 Xaa_8 Xaa_9 Xaa_{10}
Xaa_{11} Xaa_{12} Xaa_{13} Xaa_{14} Xaa_{15} Xaa_{16} Xaa_{17} Ala Xaa_{19} Xaa_{20}
Xaa_{21} Xaa_{22} Xaa_{23} Xaa_{24} Xaa_{25} Xaa_{26} Xaa_{27} Xaa_{28}-Z_1; wherein

Xaa_1 is His, Arg, Tyr, Ala, Norval, Val or Norleu;
Xaa_2 is Ser, Gly, Ala or Thr;
Xaa_3 is Ala, Asp or Glu;
Xaa_4 is Ala, Norval, Val, Norleu or Gly;
Xaa_5 is Ala or Thr;
Xaa_6 is Phe, Tyr or naphthylalanine;

Xaa_7 is Thr or Ser;

Xaa_8 is Ala, Ser or Thr;

Xaa_9 is Ala, Norval, Val, Norleu, Asp or Glu;

Xaa_{10} is Ala, Leu, Ile, Val, pentylglycine or Met;

Xaa_{11} is Ala or Ser;

Xaa_{12} is Ala or Lys;

Xaa_{13} is Ala or Gln;

Xaa_{14} is Ala, Leu, Ile, pentylglycine, Val or Met;

Xaa_{15} is Ala or Glu;

Xaa_{16} is Ala or Glu;

Xaa_{17} is Ala or Glu;

Xaa_{19} is Ala or Val;

Xaa_{20} is Ala or Arg;

Xaa_{21} is Ala or Leu;

Xaa_{22} is Phe, Tyr or naphthylalanine;

Xaa_{23} is Ile, Val, Leu, pentylglycine, tert-butylglycine or Met;

Xaa_{24} is Ala, Glu or Asp;

Xaa_{25} is Ala, Trp, Phe, Tyr or naphthylalanine;

Xaa_{26} is Ala or Leu;

Xaa_{27} is Ala or Lys;

Xaa_{28} is Ala or Asn;

Z_1 is -OH,

$-NH_2$,

Gly-Z_2,

Gly Gly-Z_2,

Gly Gly Xaa_{31}-Z_2,

Gly Gly Xaa_{31} Ser-Z_2,

Gly Gly Xaa_{31} Ser Ser-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly Ala-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36}-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36} Xaa_{37}-Z_2,

Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36} Xaa_{37} Xaa_{38}-Z_2 or Gly Gly Xaa_{31} Ser Ser Gly Ala Xaa_{36} Xaa_{37} Xaa_{38} Xaa_{39}-Z_2; wherein

Xaa_{31}, Xaa_{36}, Xaa_{37} and Xaa_{38} are independently Pro, homoproline, 3Hyp, 4Hyp, thioproline, N-alkylglycine, N-alkylpentylglycine or N-alkylalanine; and

Z_2 is -OH or $-NH_2$;

provided that no more than three of Xaa_3, Xaa_4, Xaa_5, Xaa_6, Xaa_8, Xaa_9, Xaa_{10}, Xaa_{11}, Xaa_{12}, Xaa_{13}, Xaa_{14}, Xaa_{15}, Xaa_{16}, Xaa_{17}, Xaa_{19}, Xaa_{20}, Xaa_{21}, Xaa_{24}, Xaa_{25}, Xaa_{26}, Xaa_{27} and Xaa_{28} are Ala; and provided also that, if Xaa_1 is His, Arg or Tyr, then at least one of Xaa_3, Xaa_4 and Xaa_9 is Ala.

Definitions

In accordance with the present invention and as used herein, the following terms are defined to have the following meanings, unless explicitly stated otherwise.

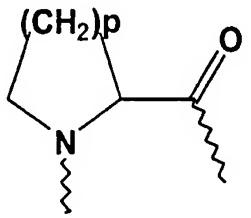
The term "amino acid" refers to natural amino acids, unnatural amino acids, and amino acid analogs, all in their D and L stereoisomers if their structure allow such stereoisomeric forms. Natural amino acids include alanine (Ala), arginine (Arg), asparagine (Asn), aspartic acid (Asp), cysteine (Cys), glutamine (Gln), glutamic acid (Glu), glycine (Gly), histidine (His), isoleucine (Ile),

leucine (Leu), Lysine (Lys), methionine (Met), phenylalanine (Phe), proline (Pro), serine (Ser), threonine (Thr), typtophan (Trp), tyrosine (Tyr) and valine (Val). Unnatural amino acids include, but are not limited to azetidinecarboxylic acid, 2-aminoadipic acid, 3-aminoadipic acid, beta-alanine, aminopropionic acid, 2-aminobutyric acid, 4-aminobutyric acid, 6-aminocaproic acid, 2-aminoheptanoic acid, 2-aminoisobutyric acid, 3-aminoisbutyric acid, 2-aminopimelic acid, tertiary-butylglycine, 2,4-diaminoisobutyric acid, desmosine, 2,2'-diaminopimelic acid, 2,3-diaminopropionic acid, N-ethylglycine, N-ethylasparagine, homoproline, hydroxylysine, allo-hydroxylysine, 3-hydroxyproline, 4-hydroxyproline, isodesmosine, allo-isoleucine, N-methylalanine, N-methylglycine, N-methylisoleucine, N-methylpentylglycine, N-methylvaline, naphthalanine, norvaline, norleucine, ornithine, pentylglycine; pipecolic acid and thioproline. Amino acid analogs include the natural and unnatural amino acids which are chemically blocked, reversibly or irreversibly, or modified on their N-terminal amino group or their side-chain groups, as for example, methionine sulfoxide, methionine sulfone, S-(carboxymethyl)-cysteine, S-(carboxymethyl)-cysteine sulfoxide and S-(carboxymethyl)-cysteine sulfone.

The term "amino acid analog" refers to an amino acid wherein either the C-terminal carboxy group, the N-terminal amino group or side-chain functional group has been chemically codified to another functional group. For example, aspartic acid-(beta-methyl ester) is an amino

acid analog of aspartic acid; N-ethylglycine is an amino acid analog of glycine; or alanine carboxamide is an amino acid analog of alanine.

The term "amino acid residue" refers to radicals having the structure: (1) -C(O)-R-NH-, wherein R typically is -CH(R')-, wherein R' is an amino acid side chain, typically H or a carbon containing substitutent; or (2),



wherein p is 1, 2 or 3 representing the azetidinecarboxylic acid, proline or pipecolic acid residues, respectively.

The term "lower" referred to herein in connection with organic radicals such as alkyl groups defines such groups with up to and including about 6, preferably up to and including 4 and advantageously one or two carbon atoms. Such groups may be straight chain or branched chain.

"Pharmaceutically acceptable salt" includes salts of the compounds described herein derived from the combination of such compounds and an organic or inorganic acid. In practice the use of the salt form amounts to use of the base form. The compounds are useful in both free base and salt form.

In addition, the following abbreviations stand for the following:

"ACN" or "CH_3CN" refers to acetonitrile.

"Boc", "tBoc" or "Tboc" refers to t-butoxy carbonyl.

"DCC" refers to N,N'-dicyclohexylcarbodiimide.

"Fmoc" refers to fluorenylmethoxycarbonyl.

"HBTU" refers to 2-(1H-benzotriazol-1-yl)-1,1,3,3,-tetramethyluronium hexaflurophosphate.

"HOBt" refers to 1-hydroxybenzotriazole monohydrate.

"homoP" or hPro" refers to homoproline.

"MeAla" or "Nme" refers to N-methylalanine.

"naph" refers to naphthylalanine.

"pG" or pGly" refers to pentylglycine.

"tBuG" refers to tertiary-butylglycine.

"ThioP" or tPro" refers to thioproline.

3Hyp" refers to 3-hydroxyproline

4Hyp" refers to 4-hydroxyproline

NAG" refers to N-alkylglycine

NAPG" refers to N-alkylpentylglycine

"Norval" refers to norvaline

"Norleu" refers to norleucine

Preparation of Compounds

The exendins and exendin agonists described herein may be prepared using standard solid-phase peptide synthesis techniques and preferably an automated or semiautomated peptide synthesizer. Typically, using such

techniques, an α-N-carbamoyl protected amino acid and an amino acid attached to the growing peptide chain on a resin are coupled at room temperature in an inert solvent such as dimethylformamide, N-methylpyrrolidinone or methylene chloride in the presence of coupling agents such as dicyclohexylcarbodiimide and 1-hydroxybenzotriazole in the presence of a base such as diisopropylethylamine. The α-N-carbamoyl protecting group is removed from the resulting peptide-resin using a reagent such as trifluoroacetic acid or piperidine, and the coupling reaction repeated with the next desired N-protected amino acid to be added to the peptide chain. Suitable N-protecting groups are well known in the art, with t-butyloxycarbonyl (tBoc) and fluorenylmethoxycarbonyl (Fmoc) being preferred herein.

The solvents, amino acid derivatives and 4-methylbenzhydryl-amine resin used in the peptide synthesizer may be purchased from Applied Biosystems Inc. (Foster City, CA). The following side-chain protected amino acids may be purchased from Applied Biosystems, Inc.: Boc-Arg(Mts), Fmoc-Arg(Pmc), Boc-Thr(Bzl), Fmoc-Thr(t-Bu), Boc-Ser(Bzl), Fmoc-Ser(t-Bu), Boc-Tyr(BrZ), Fmoc-Tyr(t-Bu), Boc-Lys(Cl-Z), Fmoc-Lys(Boc), Boc-Glu(Bzl), Fmoc-Glu(t-Bu), Fmoc-His(Trt), Fmoc-Asn(Trt), and Fmoc-Gln(Trt). Boc-His(BOM) may be purchased from Applied Biosystems, Inc. or Bachem Inc. (Torrance, CA). Anisole, dimethylsulfide, phenol, ethanedithiol, and thioanisole may be obtained from

Aldrich Chemical Company (Milwaukee, WI). Air Products and Chemicals (Allentown, PA) supplies HF. Ethyl ether, acetic acid and methanol may be purchased from Fisher Scientific (Pittsburgh, PA).

Solid phase peptide synthesis may be carried out with an automatic peptide synthesizer (Model 430A, Applied Biosystems Inc., Foster City, CA) using the NMP/HOBt (Option 1) system and tBoc or Fmoc chemistry (see, Applied Biosystems User's Manual for the ABI 430A Peptide Synthesizer, Version 1.3B July 1, 1988, section 6, pp. 49-70, Applied Biosystems, Inc., Foster City, CA) with capping. Boc-peptide-resins may be cleaved with HF (-5° C to 0° C, 1 hour). The peptide may be extracted from the resin with alternating water and acetic acid, and the filtrates lyophilized. The Fmoc-peptide resins may be cleaved according to standard methods (Introduction to Cleavage Techniques, Applied Biosystems, Inc., 1990, pp. 6-12). Peptides may be also be assembled using an Advanced Chem Tech Synthesizer (Model MPS 350, Louisville, Kentucky).

Peptides may be purified by RP-HPLC (preparative and analytical) using a Waters Delta Prep 3000 system. A C4, C8 or C18 preparative column (10μ , 2.2 x 25 cm; Vydac, Hesperia, CA) may be used to isolate peptides, and purity may be determined using a C4, C8 or C18 analytical column (5μ , 0.46 x 25 cm; Vydac). Solvents (A=0.1% TFA/water and B=0.1% TFA/CH_3CN) may be delivered to the analytical column at a flowrate of 1.0 ml/min and to the preparative column at 15 ml/min. Amino acid analyses may be performed

on the Waters Pico Tag system and processed using the Maxima program. Peptides may be hydrolyzed by vapor-phase acid hydrolysis (115° C, 20-24 h). Hydrolysates may be derivatized and analyzed by standard methods (Cohen, et al., The Pico Tag Method: A Manual of Advanced Techniques for Amino Acid Analysis, pp. 11-52, Millipore Corporation, Milford, MA (1989)). Fast atom bombardment analysis may be carried out by M-Scan, Incorporated (West Chester, PA). Mass calibration may be performed using cesium iodide or cesium iodide/glycerol. Plasma desorption ionization analysis using time of flight detection may be carried out on an Applied Biosystems Bio-Ion 20 mass spectrometer. Electrospray mass spectroscopy may be carried out on a VG-Trio machine.

Peptide compounds useful in the invention may also be prepared using recombinant DNA techniques, using methods now known in the art. See, e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual, 2d Ed., Cold Spring Harbor (1989). Non-peptide compounds useful in the present invention may be prepared by art-known methods. For example, phosphate-containing amino acids and peptides containing such amino acids, may be prepared using methods known in the art. See, e.g., Bartlett and Landen, Biorg. Chem. 14:356-377 (1986).

The compounds described above are useful in view of their pharmacological properties. In particular, the compounds of the invention possess activity as agents to reduce food intake. They can be used to treat conditions or diseases which can be alleviated by reducing food

intake.

Compositions useful in the invention may conveniently be provided in the form of formulations suitable for parenteral (including intravenous, intramuscular and subcutaneous) or nasal or oral administration. In some cases, it will be convenient to provide an exendin or exendin agonist and another food-intake-reducing, plasma glucose-lowering or plasma lipid-lowering agent, such as amylin, an amylin agonist, a CCK, or a leptin, in a single composition or solution for administration together. In other cases, it may be more advantageous to administer the additional agent separately from said exendin or exendin agonist. A suitable administration format may best be determined by a medical practitioner for each patient individually. Suitable pharmaceutically acceptable carriers and their formulation are described in standard formulation treatises, e.g., Remington's Pharmaceutical Sciences by E.W. Martin. See also Wang, Y.J. and Hanson, M.A. "Parenteral Formulations of Proteins and Peptides: Stability and Stabilizers," Journal of Parenteral Science and Technology, Technical Report No. 10, Supp. 42:2S (1988).

Compounds useful in the invention can be provided as parenteral compositions for injection or infusion. They can, for example, be suspended in an inert oil, suitably a vegetable oil such as sesame, peanut, olive oil, or other acceptable carrier. Preferably, they are suspended in an aqueous carrier, for example, in an isotonic buffer solution at a pH of about 3.0 to 8.0, preferably at a pH of

about 3.5 to 5.0. These compositions may be sterilized by conventional sterilization techniques, or may be sterile filtered. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions, such as pH buffering agents. Useful buffers include for example, sodium acetate/acetic acid buffers. A form of repository or "depot" slow release preparation may be used so that therapeutically effective amounts of the preparation are delivered into the bloodstream over many hours or days following transdermal injection or delivery.

The desired isotonicity may be accomplished using sodium chloride or other pharmaceutically acceptable agents such as dextrose, boric acid, sodium tartrate, propylene glycol, polyols (such as mannitol and sorbitol), or other inorganic or organic solutes. Sodium chloride is preferred particularly for buffers containing sodium ions.

The claimed compositions can also be formulated as pharmaceutically acceptable salts (*e.g.*, acid addition salts) and/or complexes thereof. Pharmaceutically acceptable salts are non-toxic salts at the concentration at which they are administered. The preparation of such salts can facilitate the pharmacological use by altering the physical-chemical characteristics of the composition without preventing the composition from exerting its physiological effect. Examples of useful alterations in physical properties include lowering the melting point to facilitate transmucosal administration and increasing the solubility to facilitate the administration of higher

concentrations of the drug.

Pharmaceutically acceptable salts include acid addition salts such as those containing sulfate, hydrochloride, phosphate, sulfamate, acetate, citrate, lactate, tartrate, methanesulfonate, ethanesulfonate, benzenesulfonate, *p*-toluenesulfonate, cyclohexylsulfamate and quinate. Pharmaceutically acceptable salts can be obtained from acids such as hydrochloric acid, sulfuric acid, phosphoric acid, sulfamic acid, acetic acid, citric acid, lactic acid, tartaric acid, malonic acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, *p*-toluenesulfonic acid, cyclohexylsulfamic acid, and quinic acid. Such salts may be prepared by, for example, reacting the free acid or base forms of the product with one or more equivalents of the appropriate base or acid in a solvent or medium in which the salt is insoluble, or in a solvent such as water which is then removed in vacuo or by freeze-drying or by exchanging the ions of an existing salt for another ion on a suitable ion exchange resin.

Carriers or excipients can also be used to facilitate administration of the compound. Examples of carriers and excipients include calcium carbonate, calcium phosphate, various sugars such as lactose, glucose, or sucrose, or types of starch, cellulose derivatives, gelatin, vegetable oils, polyethylene glycols and physiologically compatible solvents. The compositions or pharmaceutical composition can be administered by different routes including intravenously, intraperitoneal, subcutaneous, and intramuscular, orally, topically, transmucosally, or by

pulmonary inhalation.

If desired, solutions of the above compositions may be thickened with a thickening agent such as methyl cellulose. They may be prepared in emulsified form, either water in oil or oil in water. Any of a wide variety of pharmaceutically acceptable emulsifying agents may be employed including, for example, acacia powder, a non-ionic surfactant (such as a Tween), or an ionic surfactant (such as alkali polyether alcohol sulfates or sulfonates, e.g., a Triton).

Compositions useful in the invention are prepared by mixing the ingredients following generally accepted procedures. For example, the selected components may be simply mixed in a blender or other standard device to produce a concentrated mixture which may then be adjusted to the final concentration and viscosity by the addition of water or thickening agent and possibly a buffer to control pH or an additional solute to control tonicity.

For use by the physician, the compositions will be provided in dosage unit form containing an amount of an exendin or exendin agonist, for example, exendin-3, and/or exendin-4, with or without another food intake-reducing, plasma glucose-lowering or plasma lipid-lowering agent. Therapeutically effective amounts of an exendin or exendin agonist for use in reducing food intake are those that suppress appetite at a desired level. As will be recognized by those in the field, an effective amount of therapeutic agent will vary with many factors including the age and weight of the patient, the patient's physical

condition, the blood sugar level and other factors.

The effective daily appetite-suppressing dose of the compounds will typically be in the range of about 10 to 30 μg to about 5 mg/day, preferably about 10 to 30 μg to about 2 mg/day and more preferably about 10 to 100 μg to about 1 mg/day, most preferably about 30 μg to about 500 μg/day, for a 70 kg patient, administered in a single or divided doses. The exact dose to be administered is determined by the attending clinician and is dependent upon where the particular compound lies within the above quoted range, as well as upon the age, weight and condition of the individual. Administration should begin whenever the suppression of food intake, or weight lowering is desired, for example, at the first sign of symptoms or shortly after diagnosis of obesity, diabetes mellitus, or insulin-resistance syndrome. Administration may be by injection, preferably subcutaneous or intramuscular. Orally active compounds may be taken orally, however dosages should be increased 5-10 fold.

The optimal formulation and mode of administration of compounds of the present application to a patient depend on factors known in the art such as the particular disease or disorder, the desired effect, and the type of patient. While the compounds will typically be used to treat human subjects they may also be used to treat similar or identical diseases in other vertebrates such as other primates, farm animals such as swine, cattle and poultry, and sports animals and pets such as horses, dogs and cats.

To assist in understanding the present invention, the following Examples are included. The experiments relating to this invention should not, of course, be construed as specifically limiting the invention and such variations of the invention, now known or later developed, which would be within the purview of one skilled in the art are considered to fall within the scope of the invention as described herein and hereinafter claimed.

EXAMPLE 1: Exendin Injections Reduced the Food Intake of Normal Mice

All mice (NIH:Swiss mice) were housed in a stable environment of 22 (± 2)° C, 60 (±10) % humidity and a 12:12 light:dark cycle; with lights on at 0600. Mice were housed in groups of four in standard cages with *ad libitum* access to food (Teklad: LM 485; Madison, WI) and water except as noted, for at least two weeks before the experiments.

All experiments were conducted between the hours of 0700 and 0900. The mice were food deprived (food removed at 1600 hr from all animals on day prior to experiment) and individually housed. All mice received an intraperitoneal injection (5 μl/kg) of either saline or exendin-4 at doses of 0.1, 1.0, 10 and 100 μg/kg and were immediately presented with a pre-weighed food pellet (Teklad LM 485). The food pellet was weighed at 30-minute, 1-hr, 2-hr and 6-hr intervals to determine the amount of food eaten.

Figure 1 depicts cumulative food intake over periods of 0.5, 1, 2 and 6hr in overnight-fasted normal NIH:Swiss

mice following ip injection of saline, 2 doses of GLP-1, or 4 doses of exendin-4. At doses up to 100μg/kg, GLP-1 had no effect on food intake measured over any period, a result consistent with that previously reported (Bhavsar, S.P., et al., Soc. Neurosci. Abstr. 21:460 (188.8) (1995); and Turton, M.D., Nature, 379:69-72, (1996)).

In contrast, exendin-4 injections potently and dose-dependently inhibited food intake. The ED_{50} for inhibition of food intake over 30 min was 1μg/kg, which is a level about as potent as amylin (ED_{50} 3.6μg/kg) or the prototypical peripheral satiety agent, CCK (ED_{50} 0.97μg/kg) as measured in this preparation. However, in contrast to the effects of amylin or CCK, which abate after 1-2 hours, the inhibition of food intake with exendin-4 was still present after at least 6 hours after injection.

EXAMPLE 2: Exendin Reduced the Food Intake of Obese Mice

All mice (female ob/ob mice) were housed in a stable environment of 22 (±2)° C, 60 (±10) % humidity and a 12:12 light:dark cycle; with lights on at 0600. Mice were housed in groups of four in standard cages with *ad libitum* access to food (Teklad: LM 485) and water except as noted, for at least two weeks before the experiments.

All experiments were conducted between the hours of 0700 and 0900. The mice were food deprived (food removed at 1600 hr from all animals on day prior to experiment) and individually housed. All mice received an intraperitoneal injection (5 μl/kg) of either saline or exendin-4 at doses

of 0.1, 1.0 and 10 μg/kg (female ob/ob mice) and were immediately presented with a pre-weighed food pellet (Teklad LM 485). The food pellet was weighed at 30-minute, 1 -hr, 2-hr and 6-hr intervals to determine the amount of food eaten.

Figure 2 depicts the effect of exendin-4 in the ob/ob mouse model of obesity. The obese mice had a similar food intake-related response to exendin as the normal mice. Moreover, the obese mice were not hypersensitive to exendin, as has been observed with amylin and leptin (Young, A.A., et al., Program and Abstracts, 10th International Congress of Endocrinology, June 12-15, 1996 San Francisco, pg 419 (P2-58)).

EXAMPLE 3: Intracerebroventricular Injections of Exendin Inhibited Food Intake in Rats

All rats (Harlan Sprague-Dawley) were housed in a stable environment of 22 (±2)° C, 60 (±10)% humidity and a 12:12 light:dark cycle; with lights on at 0600. Rats were obtained from Zivic Miller with an intracerebroventricular cannula (ICV cannula) implanted (coordinates determined by actual weight of animals and referenced to Paxinos, G. and Watson, C. "The Rat Brain in stereotaxic coordinates," second edition. Academic Press) and were individually housed in standard cages with *ad libitum* access to food (Teklad: LM 485) and water for at least one week before the experiments.

All injections were given between the hours of 1700

and 1800. The rats were habituated to the ICV injection procedure at least once before the ICV administration of compound. All rats received an ICV injection (2 μl/30 seconds) of either saline or exendin-4 at doses of 0.01, 0.03, 0.1, 0.3, and 1.0 μg. All animals were then presented with pre-weighed food (Teklad LM 485) at 1800, when the lights were turned off. The amount of food left was weighed at 2-hr, 12-hr and 24-hr intervals to determine the amount of food eaten by each animal.

Figure 3 depicts a dose-dependent inhibition of food intake in rats that received doses greater than 0.1μg/rat. The ED_{50} was ≈ 0.1μg, exendin-4 is thus ≈100-fold more potent than intracerebroventricular injections of GLP-1 as reported by Turton, M.D., et al. (Nature 379:69-72 (1996)).

EXAMPLE 4: Exendin Agonists Reduced the Food Intake in Mice

All mice (NIH:Swiss mice) were housed in a stable environment of 22 (±2)° C, 60 (±10) % humidity and a 12:12 light:dark cycle; with lights on at 0600. Mice were housed in groups of four in standard cages with *ad libitum* access to food (Teklad: LM 485; Madison, WI) and water except as noted, for at least two weeks before the experiments.

All experiments were conducted between the hours of 0700 and 0900. The mice were food deprived (food removed at 1600 hr from all animals on day prior to experiment) and individually housed. All mice received an

intraperitoneal injection (5 μl/kg) of either saline or test compound at doses of 1, 10, and 100 μg/kg and immediately presented with a food pellet (Teklad LM 485). The food pellet was weighed at 30-minute, 1-hr, 2-hr and 6-hr intervals to determine the amount of food eaten.

Figure 4 depicts the cumulative food intake over periods of 0.5, 1, 2 and 6 hr in overnight-fasted normal NIH:Swiss mice following ip injection of saline or exendin-4 (1-30) ("Compound 1") in doses of 1, 10 and 100 μg/kg.

Figure 5 depicts the cumulative food intake over periods of 0.5, 1, 2 and 6 hr in overnight-fasted normal NIH:Swiss mice following ip injection of saline or exendin-4 (1-30) amide ("Compound 2") in doses of 1, 10 and 100 μg/kg.

Figure 6 depicts the cumulative food intake over periods of 0.5, 1, 2 and 6 hr in overnight-fasted normal NIH:Swiss mice following ip injection of saline or exendin-4 (1-28) amide ("Compound 3") in doses of 1, 10 and 100 μg/kg.

Figure 7 depicts the cumulative food intake over periods of 0.5, 1, 2 and 6 hr in overnight-fasted normal NIH:Swiss mice following ip injection of saline or ^{14}Leu,^{25}Phe exendin-4 amide ("Compound 4") in doses of 1, 10 and 100 μg/kg.

Figure 8 depicts the cumulative food intake over periods of 0.5, 1, 2 and 6 hr in overnight-fasted normal NIH:Swiss mice following ip injection of saline or ^{14}Leu,^{25}Phe exendin-4 (1-28) amide ("Compound 5") in doses

of 1, 10 and 100 μg/kg.

Figure 9 depicts the cumulative food intake over periods of 0.5, 1, 2 and 6 hr in overnight-fasted normal NIH:Swiss mice following ip injection of saline or ^{14}Leu,^{22}Ala,^{25}Phe exendin-4 (1-28) amide ("Compound 6") in doses of 1, 10 and 100 μg/kg.

EXAMPLE 5

Preparation of amidated peptide having SEQ. ID. NO. 9

The above-identified peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.). In general, single-coupling cycles were used throughout the synthesis and Fast Moc (HBTU activation) chemistry was employed. However, at some positions coupling was less efficient than expected and double couplings were required. In particular, residues Asp_9, Thr, and Phe_6 all required double coupling. Deprotection (Fmoc group removal)of the growing peptide chain using piperidine was not always efficient. Double deprotection was required at positions Arg_{20}, Val_{19} and Leu_{14}. Final deprotection of the completed peptide resin was achieved using a mixture of triethylsilane (0.2 mL), ethanedithiol (0.2 mL), anisole (0.2 mL), water (0.2 mL) and trifluoroacetic acid (15 mL) according to standard methods (Introduction to Cleavage Techniques, Applied Biosystems, Inc.) The peptide was precipitated in ether/water (50 mL) and centrifuged. The

precipitate was reconstituted in glacial acetic acid and lyophilized. The lyophilized peptide was dissolved in water). Crude purity was about 55%.

Used in purification steps and analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN).

The solution containing peptide was applied to a preparative C-18 column and purified (10% to 40% Solvent B in Solvent A over 40 minutes). Purity of fractions was determined isocratically using a C-18 analytical column. Pure fractions were pooled furnishing the above-identified peptide. Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 14.5 minutes. Electrospray Mass Spectrometry (M): calculated 4131.7; found 4129.3.

EXAMPLE 6

Preparation of Peptide having SEQ. ID. NO. 10

The above-identified peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 25% to 75% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 21.5

minutes. Electrospray Mass Spectrometry (M): calculated 4168.6; found 4171.2.

EXAMPLE 7

Preparation of Peptide having SEQ. ID. NO. 11

The above-identified peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 17.9 minutes. Electrospray Mass Spectrometry (M): calculated 4147.6; found 4150.2.

EXAMPLE 8

Preparation of Peptide having SEQ. ID. NO. 12

The above-identified peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN).

Analytical RP-HPLC (gradient 35% to 65% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 19.7 minutes. Electrospray Mass Spectrometry (M): calculated 4212.6; found 4213.2.

EXAMPLE 9

Preparation of Peptide having SEQ. ID. NO. 13

The above-identified peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 50% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 16.3 minutes. Electrospray Mass Spectrometry (M): calculated 4262.7; found 4262.4.

EXAMPLE 10

Preparation of Peptide having SEQ. ID. NO. 14

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.),

cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4172.6

EXAMPLE 11

Preparation of Peptide having SEQ. ID. NO. 15

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4224.7.

EXAMPLE 12

Preparation of Peptide having SEQ. ID. NO. 16

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4172.6

EXAMPLE 13

Preparation of Peptide having SEQ. ID. NO. 17

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is

then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4186.6

EXAMPLE 14

Preparation of Peptide having SEQ. ID. NO. 18

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4200.7

EXAMPLE 15

Preparation of Peptide having SEQ. ID. NO. 19

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A

(0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4200.7

EXAMPLE 16

Preparation of Peptide having SEQ. ID. NO. 20

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4202.7.

EXAMPLE 17

Preparation of Peptide having SEQ. ID. NO. 21

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using

Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4145.6.

EXAMPLE 18

Preparation of Peptide having SEQ. ID. NO. 22

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4184.6.

EXAMPLE 19

Preparation of Peptide having SEQ. ID. NO. 23

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4145.6.

EXAMPLE 20

Preparation of Peptide having SEQ. ID. NO. 24

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in

Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4224.7.

EXAMPLE 21

Preparation of Peptide having SEQ. ID. NO. 25

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4172.6.

EXAMPLE 22

Preparation of Peptide having SEQ. ID. NO. 26

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a

similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4115.5.

EXAMPLE 23

Preparation of Peptide having SEQ. ID. NO. 27

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4188.6.

EXAMPLE 24

Preparation of Peptide having SEQ. ID. NO. 28

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4131.6.

EXAMPLE 25

Preparation of Peptide having SEQ. ID. NO. 29

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the

product peptide. Electrospray Mass Spectrometry (M): calculated 4172.6.

EXAMPLE 26

Preparation of Peptide having SEQ. ID. NO. 30

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4145.6.

EXAMPLE 27

Preparation of Peptide having SEQ. ID. NO. 31

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the thioproline positions 38, 37, 36 and 31.

Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4266.8.

EXAMPLE 28

Preparation of Peptide having SEQ. ID. NO. 32

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the thioproline positions 38, 37 and 36. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4246.8.

EXAMPLE 29

Preparation of Peptide having SEQ. ID. NO. 33

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide

norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the homoproline positions 38, 37, 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4250.8.

EXAMPLE 30

Preparation of Peptide having SEQ. ID. NO. 34

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the homoproline positions 38, 37, and 36. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4234.8.

EXAMPLE 31

Preparation of Peptide having SEQ. ID. NO. 35

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the thioproline positions 38, 37, 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4209.8.

EXAMPLE 32

Preparation of Peptide having SEQ. ID. NO. 36

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the homoproline positions 38, 37, 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and

Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4193.7.

EXAMPLE 33

Preparation of Peptide having SEQ. ID. NO. 37

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the N-methylalanine positions 38, 37, 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3858.2.

EXAMPLE 34

Preparation of Peptide having SEQ. ID. NO. 38

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using

Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the N-methylalanine positions 38, 37 and 36. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3940.3.

EXAMPLE 35

Preparation of Peptide having SEQ. ID. NO. 39

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Additional double couplings are required at the N-methylalanine positions 38, 37, 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3801.1.

EXAMPLE 36

Preparation of C-terminal carboxylic acid Peptides corresponding to the above C-terminal amide sequences.

The above peptides of Examples 5 to 35 are assembled on the so called Wang resin (p-alkoxybenzylalacohol resin (Bachem, 0.54 mmole/g)) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 5. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry provides an experimentally determined (M).

EXAMPLE 37

Preparation of Peptide having SEQ ID NO. 7

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly-NH_2 [SEQ. ID. NO. 7]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.). In general, single-coupling cycles were used throughout the

synthesis and Fast Moc (HBTU activation) chemistry was employed. Deprotection (Fmoc group removal)of the growing peptide chain was achieved using piperidine. Final deprotection of the completed peptide resin was achieved using a mixture of triethylsilane (0.2 mL), ethanedithiol (0.2 mL), anisole (0.2 mL), water (0.2 mL) and trifluoroacetic acid (15 mL) according to standard methods (Introduction to Cleavage Techniques, Applied Biosystems, Inc.) The peptide was precipitated in ether/water (50 mL) and centrifuged. The precipitate was reconstituted in glacial acetic acid and lyophilized. The lyophilized peptide was dissolved in water). Crude purity was about 75%.

Used in purification steps and analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). The solution containing peptide was applied to a preparative C-18 column and purified (10% to 40% Solvent B in Solvent A over 40 minutes). Purity of fractions was determined isocratically using a C-18 analytical column. Pure fractions were pooled furnishing the above-identified peptide. Analytical RP-HPLC (gradient 30% to 50% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 18.9 minutes. Electrospray Mass Spectrometry (M): calculated 3408.0; found 3408.9.

EXAMPLE 38

Preparation of Peptide having SEQ ID NO. 40

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 40]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 40% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 17.9 minutes. Electrospray Mass Spectrometry (M): calculated 3294.7; found 3294.8.

EXAMPLE 39

Preparation of Peptide having SEQ ID NO. 41

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 41]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 29% to 36% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 20.7 minutes. Electrospray Mass Spectrometry (M): calculated 3237.6; found 3240.

EXAMPLE 40

Preparation of Peptide having SEQ ID NO. 42

His Ala Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 42]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN).

Analytical RP-HPLC (gradient 36% to 46% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 15.2 minutes. Electrospray Mass Spectrometry (M): calculated 3251.6; found 3251.5.

EXAMPLE 41

Preparation of Peptide having SEQ ID NO. 43

His Gly Glu Gly Ala Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 43]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 36% to 46% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 13.1 minutes. Electrospray Mass Spectrometry (M): calculated 3207.6; found 3208.3.

EXAMPLE 42

Preparation of Peptide having SEQ ID NO: 44

His Gly Glu Gly Thr Ala Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 44]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 35% to 45% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 12.8 minutes. Electrospray Mass Spectrometry (M): calculated 3161.5; found 3163.

EXAMPLE 43

Preparation of Peptide having SEQ ID NO. 45

His Gly Glu Gly Thr Phe Thr Ala Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 45]

The above-identified amidated peptide was assembled

on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 36% to 46% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 15.2 minutes. Electrospray Mass Spectrometry (M): calculated 3221.6; found 3222.7.

EXAMPLE 44

Preparation of Peptide having SEQ ID NO. 46

His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 46]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 34% to 44% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

gave product peptide having an observed retention time of 14.3 minutes. Electrospray Mass Spectrometry (M): calculated 3195.5; found 3199.4.

EXAMPLE 45

Preparation of Peptide having SEQ ID NO. 47

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ala Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 47]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 38% to 48% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 15.7 minutes. Electrospray Mass Spectrometry (M): calculated 3221.6; found 3221.6.

EXAMPLE 46

Preparation of Peptide having SEQ ID NO. 48

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Ala Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 48]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 38% to 48% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 18.1 minutes. Electrospray Mass Spectrometry (M): calculated 3180.5; found 3180.9.

EXAMPLE 47

Preparation of Peptide having SEQ ID NO. 49

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Ala Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 49]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Compound 1. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 36% to 46% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

gave product peptide having an observed retention time of 17.0 minutes. Electrospray Mass Spectrometry (M): calculated 3180.6; found 3182.8.

EXAMPLE 48

Preparation of Peptide having SEQ ID NO. 50

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Ala Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 50]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 32% to 42% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 14.9 minutes. Electrospray Mass Spectrometry (M): calculated 3195.5; found 3195.9.

EXAMPLE 49

Preparation of Peptide having SEQ ID NO. 51

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu

Ala Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 51]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 37% to 47% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 17.9 minutes. Electrospray Mass Spectrometry (M): calculated 3179.6; found 3179.0.

EXAMPLE 50

Preparation of Peptide having SEQ ID NO. 52

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Ala Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 52]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and

purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 37% to 47% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 14.3 minutes. Electrospray Mass Spectrometry (M): calculated 3179.6; found 3180.0.

EXAMPLE 51

Preparation of Peptide having SEQ ID NO. 53

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Ala Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 53]

The above-identified peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 37% to 47% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 13.7 minutes. Electrospray Mass Spectrometry (M): calculated 3179.6; found 3179.0.

EXAMPLE 52

Preparation of Peptide having SEQ ID NO. 54

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Ala Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 54]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 35% to 45% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 14.0 minutes. Electrospray Mass Spectrometry (M): calculated 3209.6; found 3212.8.

EXAMPLE 53

Preparation of Peptide having SEQ ID NO. 55

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Ala Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 55]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 38% to 48% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 14.3 minutes. Electrospray Mass Spectrometry (M): calculated 3152.5; found 3153.5.

EXAMPLE 54

Preparation of Peptide having SEQ ID NO. 56

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Ala Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 56]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 35% to 45% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

gave product peptide having an observed retention time of 12.1 minutes. Electrospray Mass Spectrometry (M): calculated 3195.5; found 3197.7.

EXAMPLE 55

Preparation of Peptide having SEQ ID NO. 57

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Ala Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 57]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 38% to 48% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 10.9 minutes. Electrospray Mass Spectrometry (M): calculated 3179.6; found 3180.5.

EXAMPLE 56

Preparation of Peptide having SEQ ID NO. 58

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Ala Leu Lys Asn-NH_2

[SEQ. ID. NO. 58]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 32% to 42% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 17.5 minutes. Electrospray Mass Spectrometry (M): calculated 3161.5; found 3163.0.

EXAMPLE 57

Preparation of Peptide having SEQ ID NO. 59

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Ala Lys Asn-NH_2 [SEQ. ID. NO. 59]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 32% to 42% Solvent B

in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 19.5 minutes. Electrospray Mass Spectrometry (M): calculated 3195.5; found 3199.

EXAMPLE 58

Preparation of Peptide having SEQ ID NO. 60

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Ala Asn-NH_2 [SEQ. ID. NO. 60]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 38% to 48% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 14.5 minutes. Electrospray Mass Spectrometry (M): calculated 3180.5; found 3183.7.

EXAMPLE 59

Preparation of Peptide having SEQ ID NO. 61

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Ala-NH_2 [SEQ. ID. NO. 61]

The above-identified amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 34% to 44% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 22.8 minutes. Electrospray Mass Spectrometry (M): calculated 3194.6; found 3197.6.

EXAMPLE 60

Preparation of Peptide having SEQ ID NO. 62

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro-NH_2 [SEQ. ID. NO. 62]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4099.6.

EXAMPLE 61

Preparation of Peptide having SEQ ID NO. 63

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro-NH_2 [SEQ. ID. NO. 63]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA

in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4042.5.

EXAMPLE 62

Preparation of Peptide having SEQ ID NO: 64

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro-NH_2 [SEQ. ID. NO. 64]

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4002.4

EXAMPLE 63

Preparation of Peptide having SEQ ID NO: 65

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro-NH_2 [SEQ. ID. NO. 65]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3945.4.

EXAMPLE 64

Preparation of Peptide having SEQ ID NO. 66

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro-NH_2 [SEQ. ID. NO. 66]

The above-identified amidated peptide is assembled on

4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3905.3.

EXAMPLE 65

Preparation of Peptide having SEQ ID NO. 67

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro-NH_2 [SEQ. ID. NO. 67]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3848.2.

EXAMPLE 66

Preparation of Peptide having SEQ ID NO. 68

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala-NH_2 [SEQ. ID. NO. 68]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3808.2.

EXAMPLE 67

Preparation of Peptide having SEQ ID NO. 69

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala-NH_2 [SEQ. ID. NO. 69]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3751.1.

EXAMPLE 68

Preparation of Peptide having SEQ ID NO. 70

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly-NH_2 [SEQ. ID. NO. 70]

The above-identified amidated peptide is assembled on

4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3737.1.

EXAMPLE 69

Preparation of Peptide having SEQ ID NO. 71

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly-NH_2 [SEQ. ID. NO. 71]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3680.1.

EXAMPLE 70

Preparation of Peptide having SEQ ID NO. 72

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser-NH_2 [SEQ. ID. NO. 72]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3680.1

EXAMPLE 71

Preparation of Peptide having SEQ ID NO. 73

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser-NH_2 [SEQ. ID. NO. 73]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3623.0.

EXAMPLE 72

Preparation of Peptide having SEQ ID NO. 74

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser-NH_2 [SEQ. ID. NO. 74]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA

in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3593.0

EXAMPLE 73

Preparation of Peptide having SEQ ID NO. 75

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser-NH_2 [SEQ. ID. NO. 75]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3535.9

EXAMPLE 74

Preparation of Peptide having SEQ ID NO. 76

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro-NH_2 [SEQ. ID. NO. 76]

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3505.9.

EXAMPLE 75

Preparation of Peptide having SEQ ID NO. 77

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro-NH_2 [SEQ. ID. NO. 77]

The above-identified amidated peptide is assembled on

4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3448.8.

EXAMPLE 76

Preparation of Peptide having SEQ ID NO. 78

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly-NH_2 [SEQ. ID. NO. 78]

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is

then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3351.7.

EXAMPLE 77

Preparation of Peptide having SEQ ID NO. 79

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly-NH_2 [SEQ. ID. NO. 79]

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3351.8.

EXAMPLE 78

Preparation of Peptide having SEQ ID NO. 80

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly-NH_2 [SEQ. ID. NO. 80]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3294.7.

EXAMPLE 79

Preparation of Peptide having SEQ ID NO. 81

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly tPro Ser Ser Gly Ala tPro tPro tPro-NH_2 [SEQ. ID. NO. 81]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Double couplings are required at residues 37,36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4197.1.

EXAMPLE 80

Preparation of Peptide having SEQ ID NO. 82

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala tPro tPro tPro-NH_2 [SEQ. ID. NO. 82]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Double couplings

are required at residues 37, 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4179.1.

EXAMPLE 81

Preparation of Peptide having SEQ ID NO. 83

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly NMeala Ser Ser Gly Ala Pro Pro-NH_2 [SEQ. ID. NO. 83]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Double couplings are required at residues 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M):

calculated 3948.3.

EXAMPLE 82

Preparation of Peptide having SEQ ID NO. 84

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly NMeala Ser Ser Gly Ala NMeala Nmeala-NH_2 [SEQ. ID. NO. 84]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Double couplings are required at residues 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3840.1.

EXAMPLE 83

Preparation of Peptide having SEQ ID NO. 85

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly hPro Ser Ser Gly Ala hPro hPro-NH_2 [SEQ. ID. NO. 85]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Double couplings are required at residues 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4050.1.

EXAMPLE 84

Preparation of Peptide having SEQ ID NO. 86

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly hPro Ser Ser Gly Ala hPro-NH_2 [SEQ. ID. NO. 86]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. A double coupling is required at residue 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3937.1

EXAMPLE 85

Preparation of Peptide having SEQ ID NO. 87

Arg Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala-NH_2 [SEQ. ID. NO. 87]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis

are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3827.2.

EXAMPLE 86

Preparation of Peptide having SEQ ID NO. 88

His Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly-NH_2 [SEQ. ID. NO. 88]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3394.8.

EXAMPLE 87

Preparation of Peptide having SEQ ID NO. 89

His Gly Glu Gly Thr Naphthylala Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 89]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3289.5.

EXAMPLE 88

Preparation of Peptide having SEQ ID NO. 90

His Gly Glu Gly Thr Phe Ser Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 90]

The above-identified amidated peptide is assembled on

4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3280.7.

EXAMPLE 89

Preparation of Peptide having SEQ ID NO. 91

His Gly Glu Gly Thr Phe Ser Thr Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 91]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3294.7.

EXAMPLE 90

Preparation of Peptide having SEQ ID NO. 92

His Gly Glu Gly Thr Phe Thr Ser Glu Leu Ser Lys Gln Met Ala Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 92]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3250.7.

EXAMPLE 91

Preparation of Peptide having SEQ ID NO. 93

His Gly Glu Gly Thr Phe Thr Ser Asp pentylgly Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys

Asn-NH_2 [SEQ. ID. NO. 93]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3253.5.

EXAMPLE 92

Preparation of Peptide having SEQ ID NO: 94

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Naphthylala Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 94]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis

are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3289.5.

EXAMPLE 93

Preparation of Peptide having SEQ ID NO. 95

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe tButylgly Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 95]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3183.4.

EXAMPLE 94

Preparation of Peptide having SEQ ID NO. 96

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Asp Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 96]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3237.6.

EXAMPLE 95

Preparation of Peptide having SEQ ID NO. 97

His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser-NH_2 [SEQ. ID. NO. 97]

The above-identified amidated peptide is assembled on

4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3637.9.

EXAMPLE 96

Preparation of Peptide having SEQ ID NO. 98

His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly-NH_2 [SEQ. ID. NO. 98]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3309.7.

EXAMPLE 97

Preparation of Peptide having SEQ ID NO. 99

His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly hPro Ser Ser Gly Ala hPro hPro-NH_2 [SEQ. ID. NO. 99]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Ecample 37. Double couplings are required at residues 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3711.1.

EXAMPLE 98

Preparation of C-terminal carboxylic acid peptides corresponding to the above C-terminal amide sequences for SEQ ID NOS. 7, 40-61, 68-75, 78-80 and 87-96

Peptides having the sequences of SEQ ID NOS. 7, 40-61, 68-75, 78-80 and 87-96 are assembled on the so called Wang resin (p-alkoxybenzylalacohol resin (Bachem, 0.54 mmole/g)) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry provides an experimentally determined (M).

EXAMPLE 99

Preparation of C-terminal carboxylic acid peptides corresponding to the above C-terminal amide sequences for SEQ ID NOS. 62-67, 76, 77 and 81-86

Peptides having the sequences of SEQ ID NOS. 62-67, 76, 77 and 81-86 are assembled on the 2-chlorotritylchloride resin (200-400 mesh), 2% DVB (Novabiochem, 0.4-1.0 mmole/g)) using Fmoc-protected amino

acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 37. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry provides an experimentally determined (M).

EXAMPLE 100

Preparation of Peptide having SEQ ID NO. 100

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 100]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.). In general, single-coupling cycles were used throughout the synthesis and Fast Moc (HBTU activation) chemistry was employed. Deprotection (Fmoc group removal)of the growing peptide chain was achieved using piperidine. Final deprotection of the completed peptide resin was achieved using a mixture of triethylsilane (0.2 mL), ethanedithiol (0.2 mL), anisole (0.2 mL), water (0.2 mL) and trifluoroacetic acid (15 mL) according to standard methods (Introduction to Cleavage Techniques, Applied Biosystems,

Inc.) The peptide was precipitated in ether/water (50 mL) and centrifuged. The precipitate was reconstituted in glacial acetic acid and lyophilized. The lyophilized peptide was dissolved in water). Crude purity was about 75%.

Used in purification steps and analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN).

The solution containing peptide was applied to a preparative C-18 column and purified (10% to 40% Solvent B in Solvent A over 40 minutes). Purity of fractions was determined isocratically using a C-18 analytical column. Pure fractions were pooled furnishing the above-identified peptide. Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 19.2 minutes. Electrospray Mass Spectrometry (M): calculated 3171.6; found 3172.

EXAMPLE 101

Preparation of Peptide having SEQ ID NO. 101

His Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 101]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.),

cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 36% to 46% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 14.9 minutes. Electrospray Mass Spectrometry (M): calculated 3179.6; found 3180.

EXAMPLE 102

Preparation of Peptide having SEQ ID NO. 102

His Gly Glu Ala Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 102]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 37% to 47% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 12.2 minutes. Electrospray Mass Spectrometry (M): calculated 3251.6; found 3253.3.

EXAMPLE 103

Preparation of Peptide having SEQ ID NO. 103

His Gly Glu Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 103]

The above amidated peptide was assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis were Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 35% to 45% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide gave product peptide having an observed retention time of 16.3 minutes. Electrospray Mass Spectrometry (M): calculated 3193.6; found 3197.

EXAMPLE 104

Preparation of Peptide having SEQ ID NO. 104

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 104]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3228.6.

EXAMPLE 105

Preparation of Peptide having SEQ ID NO. 105

His Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 105]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3234.7.

EXAMPLE 106

Preparation of Peptide having SEQ ID NO. 106

His Gly Glu Ala Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 106]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3308.7.

EXAMPLE 107

Preparation of Peptide having SEQ ID NO. 107

His Gly Glu Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2

[SEQ. ID. NO. 107]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3250.7

EXAMPLE 108

Preparation of Peptide having SEQ ID NO. 108

His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2

[SEQ. ID. NO. 108]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA

in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3252.6.

EXAMPLE 109

Preparation of Peptide having SEQ ID NO. 109

Ala Ala Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 109]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3200.6.

EXAMPLE 110

Preparation of Peptide having SEQ ID NO. 110

Ala Ala Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 110]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3143.5.

EXAMPLE 111

Preparation of Peptide having SEQ ID NO. 111

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 111]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy

acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3214.6.

EXAMPLE 112

Preparation of Peptide having SEQ ID NO. 112

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 112]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M):

calculated 3157.5.

EXAMPLE 113

Preparation of Peptide having SEQ ID NO. 113

Ala Gly Asp Gly Ala Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 113]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3184.6.

EXAMPLE 114

Preparation of Peptide having SEQ ID NO. 114

Ala Gly Asp Gly Ala Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 114]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3127.5.

EXAMPLE 115

Preparation of Peptide having SEQ ID NO. 115

Ala Gly Asp Gly Thr NaphthylAla Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 115]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B

in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3266.4.

EXAMPLE 116

Preparation of Peptide having SEQ ID NO. 116

Ala Gly Asp Gly Thr Naphthylala Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 116]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3209.4.

EXAMPLE 117

Preparation of Peptide having SEQ ID NO. 117

Ala Gly Asp Gly Thr Phe Ser Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 117]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3200.6.

EXAMPLE 118

Preparation of Peptide having SEQ ID NO. 118

Ala Gly Asp Gly Thr Phe Ser Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 118]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and

purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3143.5.

EXAMPLE 119

Preparation of Peptide having SEQ ID NO. 119

Ala Gly Asp Gly Thr Phe Thr Ala Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 119]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3198.6.

EXAMPLE 120

Preparation of Peptide having SEQ ID NO. 120

Ala Gly Asp Gly Thr Phe Thr Ala Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 120]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3141.5.

EXAMPLE 121

Preparation of Peptide having SEQ ID NO. 121

Ala Gly Asp Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 121]

The above-identified peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide

norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3170.6.

EXAMPLE 122

Preparation of Peptide having SEQ ID NO. 122

Ala Gly Asp Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 122]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M):

calculated 3113.5.

EXAMPLE 123

Preparation of Peptide having SEQ ID NO. 123

Ala Gly Asp Gly Thr Phe Thr Ser Glu Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 123]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3228.6.

EXAMPLE 124

Preparation of Peptide having SEQ ID NO. 124

Ala Gly Asp Gly Thr Phe Thr Ser Glu Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 124]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3171.6.

EXAMPLE 125

Preparation of Peptide having SEQ ID NO. 125

Ala Gly Asp Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 125]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B

in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3172.5.

EXAMPLE 126

Preparation of Peptide having SEQ ID NO. 126

Ala Gly Asp Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 126]

The above-identified amidated peptiden is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3115.4.

EXAMPLE 127

Preparation of Peptide having SEQ ID NO. 127

Ala Gly Asp Gly Thr Phe Thr Ser Asp Pentylgly Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 127]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3230.4.

EXAMPLE 128

Preparation of Peptide having SEQ ID NO. 128

Ala Gly Asp Gly Thr Phe Thr Ser Asp Pentylgly Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 128]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy

acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3198.6.

EXAMPLE 129

Preparation of Peptide having SEQ ID NO. 129

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ala Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 129]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M):

calculated 3141.5.

EXAMPLE 130

Preparation of Peptide having SEQ ID NO. 130

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ala Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 130]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3157.5.

EXAMPLE 131

Preparation of Peptide having SEQ ID NO. 131

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Ala Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 131]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3100.4.

EXAMPLE 132

Preparation of Peptide having SEQ ID NO. 132

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Ala Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 132]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B

in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3157.6.

EXAMPLE 133

Preparation of Peptide having SEQ ID NO. 133

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Ala Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 133]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3100.5.

EXAMPLE 134

Preparation of Peptide having SEQ ID NO. 134

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Ala Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 134]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3100.5.

EXAMPLE 135

Preparation of Peptide having SEQ ID NO. 135

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Ala Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 135]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and

purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3154.5.

EXAMPLE 136

Preparation of Peptide having SEQ ID NO. 136

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Ala Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 136]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3115.5.

EXAMPLE 137

Preparation of Peptide having SEQ ID NO. 137

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Pentylgly Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 137]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3212.4.

EXAMPLE 138

Preparation of Peptide having SEQ ID NO. 138

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Pentylgly Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 138]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy

acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3173.4.

EXAMPLE 139

Preparation of Peptide having SEQ ID NO. 139

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Ala Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 139]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3156.6.

EXAMPLE 140

Preparation of Peptide having SEQ ID NO. 140

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Ala Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 140]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3099.5.

EXAMPLE 141

Preparation of Peptide having SEQ ID NO. 141

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Ala Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 141]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3156.6.

EXAMPLE 142

Preparation of Peptide having SEQ ID NO. 142

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Ala Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 142]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the

product peptide. Electrospray Mass Spectrometry (M): calculated 3099.5.

EXAMPLE 143

Preparation of Peptide having SEQ ID NO. 143

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Ala Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 143]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3156.6.

EXAMPLE 144

Preparation of Peptide having SEQ ID NO. 144

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Ala Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 144]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3099.5.

EXAMPLE 145

Preparation of Peptide having SEQ ID NO. 145

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Ala Arg Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 145]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3186.6.

EXAMPLE 146

Preparation of Peptide having SEQ ID NO. 146

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Ala Arg Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 146]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3129.5.

EXAMPLE 147

Preparation of Peptide having SEQ ID NO. 147

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Ala Leu Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 147]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3129.5.

EXAMPLE 148

Preparation of Peptide having SEQ ID NO. 148

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Ala Leu Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 148]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0,55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B

in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3072.4.

EXAMPLE 149

Preparation of Peptide having SEQ ID NO. 149

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Ala Phe Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 149]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3172.5.

EXAMPLE 150

Preparation of Peptide having SEQ ID NO. 150

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Ala Phe Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 150]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3115.5.

EXAMPLE 151

Preparation of Peptide having SEQ ID NO. 151

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Naphthylala Ile Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 151]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy

acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3266.4.

EXAMPLE 152

Preparation of Peptide having SEQ ID NO. 152

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Naphthylala Ile Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 152]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M):

calculated 3209.4.

EXAMPLE 153

Preparation of Peptide having SEQ ID NO. 153

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Val Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 153]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3200.6.

EXAMPLE 154

Preparation of Peptide having SEQ ID NO. 154

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Val Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 154]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3143.5.

EXAMPLE 155

Preparation of Peptide having SEQ ID NO. 155

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe tButylgly Glu Trp Leu Lys Asn-NH_2 [SEQ. ID. NO. 155]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B

in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3216.5.

EXAMPLE 156

Preparation of Peptide having SEQ ID NO. 156

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe tButylgly Glu Phe Leu Lys Asn-NH_2 [SEQ. ID. NO. 156]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3159.4.

EXAMPLE 157

Preparation of Peptide having SEQ ID NO. 157

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met
Glu Glu Glu Ala Val Arg Leu Phe Ile Asp Trp Leu Lys Asn-NH_2
[SEQ. ID. NO. 157]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3200.6.

EXAMPLE 158

Preparation of Peptide having SEQ ID NO. 158

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu
Glu Glu Glu Ala Val Arg Leu Phe Ile Asp Phe Leu Lys Asn-NH_2
[SEQ. ID. NO. 158]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy

acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3143.5.

EXAMPLE 159

Preparation of Peptide having SEQ ID NO. 159

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Ala Leu Lys Asn-NH_2 [SEQ. ID. NO. 159]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M):

calculated 3099.5.

EXAMPLE 160

Preparation of Peptide having SEQ ID NO. 160

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Ala Leu Lys Asn-NH_2 [SEQ. ID. NO. 160]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3081.4.

EXAMPLE 161

Preparation of Peptide having SEQ ID NO. 161

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Ala Lys Asn-NH_2 [SEQ. ID. NO. 161]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3172.5.

EXAMPLE 162

Preparation of Peptide having SEQ ID NO. 162

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Ala Lys Asn-NH_2 [SEQ. ID. NO. 162]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3115.5.

EXAMPLE 163

Preparation of Peptide having SEQ ID NO. 163

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Ala Asn-NH_2 [SEQ. ID. NO. 163]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3157.5.

EXAMPLE 164

Preparation of Peptide having SEQ ID NO. 164

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Ala Asn-NH_2

[SEQ. ID. NO. 164]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3100.4.

EXAMPLE 165

Preparation of Peptide having SEQ ID NO. 165

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Ala-NH_2
[SEQ. ID. NO. 165]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA

in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3171.6.

EXAMPLE 166

Preparation of Peptide having SEQ ID NO. 166

Ala Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Ala-NH_2 [SEQ. ID. NO. 166]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3114.5.

EXAMPLE 167

Preparation of Peptide having SEQ ID NO. 167

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro-NH_2 [SEQ. ID. NO. 167]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4033.5.

EXAMPLE 168

Preparation of Peptide having SEQ ID NO. 168

His Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro-NH_2 [SEQ. ID. NO. 168]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3984.4.

EXAMPLE 169

Preparation of Peptide having SEQ ID NO. 169

His Gly Glu Ala Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro-NH_2 [SEQ. ID. NO. 169]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide

is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4016.5.

EXAMPLE 170

Preparation of Peptide having SEQ ID NO. 170

His Gly Glu Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro-NH_2 [SEQ. ID. NO. 170]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3861.3.

EXAMPLE 171

Preparation of Peptide having SEQ ID NO. 171

Ala Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn

Gly Gly Pro Ser Ser Gly Ala Pro-NH_2 [SEQ. ID. NO. 171]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3746.1.

EXAMPLE 172

Preparation of Peptide having SEQ ID NO. 172

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala-NH_2 [SEQ. ID. NO. 172]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA

in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3742.1.

EXAMPLE 173

Preparation of Peptide having SEQ ID NO. 173

His Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala-NH_2 [SEQ. ID. NO. 173]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3693.1.

EXAMPLE 174

Preparation of Peptide having SEQ ID NO. 174

His Gly Glu Ala Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly-NH_2 [SEQ. ID. NO. 174]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3751.2.

EXAMPLE 175

Preparation of Peptide having SEQ ID NO. 175

His Gly Glu Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser-NH_2 [SEQ. ID. NO. 175]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy

acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3634.1.

EXAMPLE 176

Preparation of Peptide having SEQ ID NO. 176

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser-NH_2 [SEQ. ID. NO. 176]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M):

calculated 3526.9.

EXAMPLE 177

Preparation of Peptide having SEQ ID NO. 177

His Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser-NH_2 [SEQ. ID. NO. 177]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3477.9.

EXAMPLE 178

Preparation of Peptide having SEQ ID NO. 178

His Gly Glu Ala Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro-NH_2 [SEQ. ID. NO. 178]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3519.9.

EXAMPLE 179

Preparation of Peptide having SEQ ID NO. 179

His Gly Glu Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly-NH_2 [SEQ. ID. NO. 179]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B

in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3307.7.

EXAMPLE 180

Preparation of Peptide having SEQ ID NO. 180

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly-NH_2 [SEQ. ID. NO. 180]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3186.5.

EXAMPLE 181

Preparation of Peptide having SEQ ID NO. 181

His Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly tPro Ser Ser Gly Ala tPro tPro tPro-NH_2 [SEQ. ID. NO. 181]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Double couplings are required at residues 37,36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4121.1.

EXAMPLE 182

Preparation of Peptide having SEQ ID NO. 182

His Gly Glu Ala Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala tPro tPro tPro-NH_2 [SEQ. ID. NO. 182].

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55

mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Double couplings are required at residues 37, 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4173.2.

EXAMPLE 183

Preparation of Peptide having SEQ ID NO. 183

His Gly Glu Gly Thr Phe Thr Ser Ala Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly NMeala Ser Ser Gly Ala NMeala NMeala-NH_2 [SEQ. ID. NO. 183]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Compound 1. Double couplings are required at residues 36 and 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is

then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3796.1.

EXAMPLE 184

Preparation of Peptide having SEQ ID NO. 184

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly hPro Ser Ser Gly Ala hPro-NH_2 [SEQ. ID. NO. 184]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. A double coupling is required at residue 31. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3871.1.

EXAMPLE 185

Preparation of Peptide having SEQ ID NO. 185

His Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala-NH_2 [SEQ. ID. NO. 185]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3750.2.

EXAMPLE 186

Preparation of Peptide having SEQ ID NO. 186

His Gly Asp Ala Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly-NH_2 [SEQ. ID. NO. 186]

The above-identified amdiated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy

acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 3408.8.

EXAMPLE 187

Preparation of Peptide having SEQ ID NO. 187

Ala Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro Ser-NH_2 [SEQ. ID. NO. 187]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the

product peptide. Electrospray Mass Spectrometry (M): calculated 4120.6.

EXAMPLE 188

Preparation of Peptide having SEQ ID NO. 188

Ala Gly Ala Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser Ser Gly Ala Pro Pro Pro Ser-NH_2 [SEQ. ID. NO. 188]

The above-identified amidated peptide is assembled on 4-(2'-4'-dimethoxyphenyl)-Fmoc aminomethyl phenoxy acetamide norleucine MBHA resin (Novabiochem, 0.55 mmole/g) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry (M): calculated 4005.5.

EXAMPLE 189

Preparation of C-terminal carboxylic acid peptides corresponding to the above C-terminal amide sequences for Peptides having SEQ ID NOS. 100-166, 172-177, 179-180 and 185-188.

C-terminal carboxylic acid peptides corresponding to amidated having SEQ ID NOS. 100-166, 172-177, 179-180 and 185-188 are assembled on the so called Wang resin (p-alkoxybenzylalacohol resin (Bachem, 0.54 mmole/g)) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to that described in Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry provides an experimentally determined (M).

EXAMPLE 190

Preparation of C-terminal carboxylic acid peptides corresponding to the above C-terminal amide sequences for Peptides having SEQ ID NOS. 167-171, 178 and 181-184.

C-terminal carboxylic acid eptides corresponding to amidated SEQ ID NOS. 167-171, 178 and 181-184 are assembled on the 2-chlorotritylchloride resin (200-400 mesh), 2% DVB (Novabiochem, 0.4-1.0 mmole/g)) using Fmoc-protected amino acids (Applied Biosystems, Inc.), cleaved from the resin, deprotected and purified in a similar way to that described in Example 100. Used in analysis are Solvent A (0.1% TFA in water) and Solvent B (0.1% TFA in

ACN). Analytical RP-HPLC (gradient 30% to 60% Solvent B in Solvent A over 30 minutes) of the lyophilized peptide is then carried out to determine the retention time of the product peptide. Electrospray Mass Spectrometry provides an experimentally determined (M).

Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the following claims.

WE CLAIM:

1. A method for treating conditions or disorders which can be alleviated by reducing food intake in a subject comprising administering to said subject a therapeutically effective amount of an exendin or an exendin agonist.

2. The method according to claim 1 wherein said exendin or exendin agonist is administered parenterally.

3. The method according to claim 2 wherein said parenteral administration is by injection.

4. The method according to claim 3 wherein the injection is a peripheral injection.

5. The method according to claim 1 wherein about 10 μg-30μg to about 5mg of the exendin or exendin agonist is administered per day.

6. The method according to claim 1 wherein about 10 μg-30 μg to about 2 mg of the exendin or exendin agonist is administered per day.

7. The method according to claim 1, wherein about 30 μg to about 500 μg of the exendin or exendin agonist is administered per day.

8. The method of claim 1 wherein said condition or disorder is obesity.

9. The method of claim 1 wherein said condition or disorder is Type II diabetes.

10. The method of claim 1 wherein said subject is human.

11. The method of claim 1 wherein said condition or disorder is an eating disorder.

12. The method of claim 1 wherein said condition or disorder is insulin-resistance syndrome.

13. A method for reducing the appetite of a subject comprising administering to said subject an appetite-lowering amount of an exendin or an exendin agonist.

14. A method for reducing the weight of a subject comprising administering to said subject a therapeutically effective amount of an exendin or an exendin agonist.

15. A method for lowering plasma lipids comprising administering to said subject a therapeutically effective amount of an exendin or an exendin agonist.

16. The method according to any of claims 1-15 wherein said exendin is exendin-3.

17. The method according to any of claims 1-15 wherein said exendin is exendin-4.

18. The method according to any of claims 1-15 wherein said exendin agonist is selected from the group consisting of exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28) amide, ^{14}Leu,^{25}Phe exendin-4 amide, ^{14}Leu,^{25}Phe exendin-4 (1-28) amide, and ^{14}Leu,^{22}Ala,^{25}Phe exendin-4 (1-28) amide.

19. The method according to any of claims 1-15, further comprising administering a therapeutically effective amount of one or more compounds selected from the group consisting essential of an amylin agonist, a leptin, and a CCK.

20. The method according to any of claims 1-15 wherein said exendin agonist is an exendin agonist according to Formula I.

21. The method according to any of claims 1-15 wherein said exendin agonist is an exendin agonist according to Formula II.

22. The method according to any of claims 1-15 wherein said exendin agonist is an exendin agonist according to Formula III.

23. A pharmaceutical composition for use in the treatment of conditions or disorders associated with hypernutrition comprising a therapeutically effective amount of an exendin or exendin agonist in association with a pharmaceutically acceptable carrier.

24. The pharmaceutical composition according to claim 21, wherein said exendin is exendin-3.

25. The pharmaceutical composition according to claim 21 wherein said exendin is exendin-4.

26. The pharmaceutical composition according to claim 21 wherein said exendin agonist is selected from the group consisting of exendin-4 (1-30), exendin-4 (1-30) amide, exendin-4 (1-28) amide, ^{14}Leu,^{25}Phe exendin-4 amide, ^{14}Leu,^{25}Phe exendin-4 (1-28) amide, and ^{14}Leu,^{22}Ala,^{25}Phe exendin-4 (1-28) amide.

27. The pharmaceutical composition of claim 21 wherein said therapeutically effective amount is a therapeutically effective amount for a human subject.

28. A pharmaceutical composition for use in reducing the appetite of a subject comprising a therapeutically effective amount of an exendin or exendin agonist in association with a pharmaceutically acceptable carrier.

29. A pharmaceutical composition for use in reducing the weight of a subject comprising a therapeutically effective amount of an exendin or exendin agonist in association with a pharmaceutically acceptable carrier.

30. A pharmaceutical composition for use in lowering the plasma lipid level of a subject comprising a therapeutically effective amount of an exendin or exendin agonist in association with a pharmaceutically acceptable carrier.

31. The pharmaceutical composition according to any of claims 21-28, further comprising a therapeutically effective amount of one or more compounds selected from the group consisting essentially of an amylin agonist, a leptin, and a CCK.

FIG. 1.

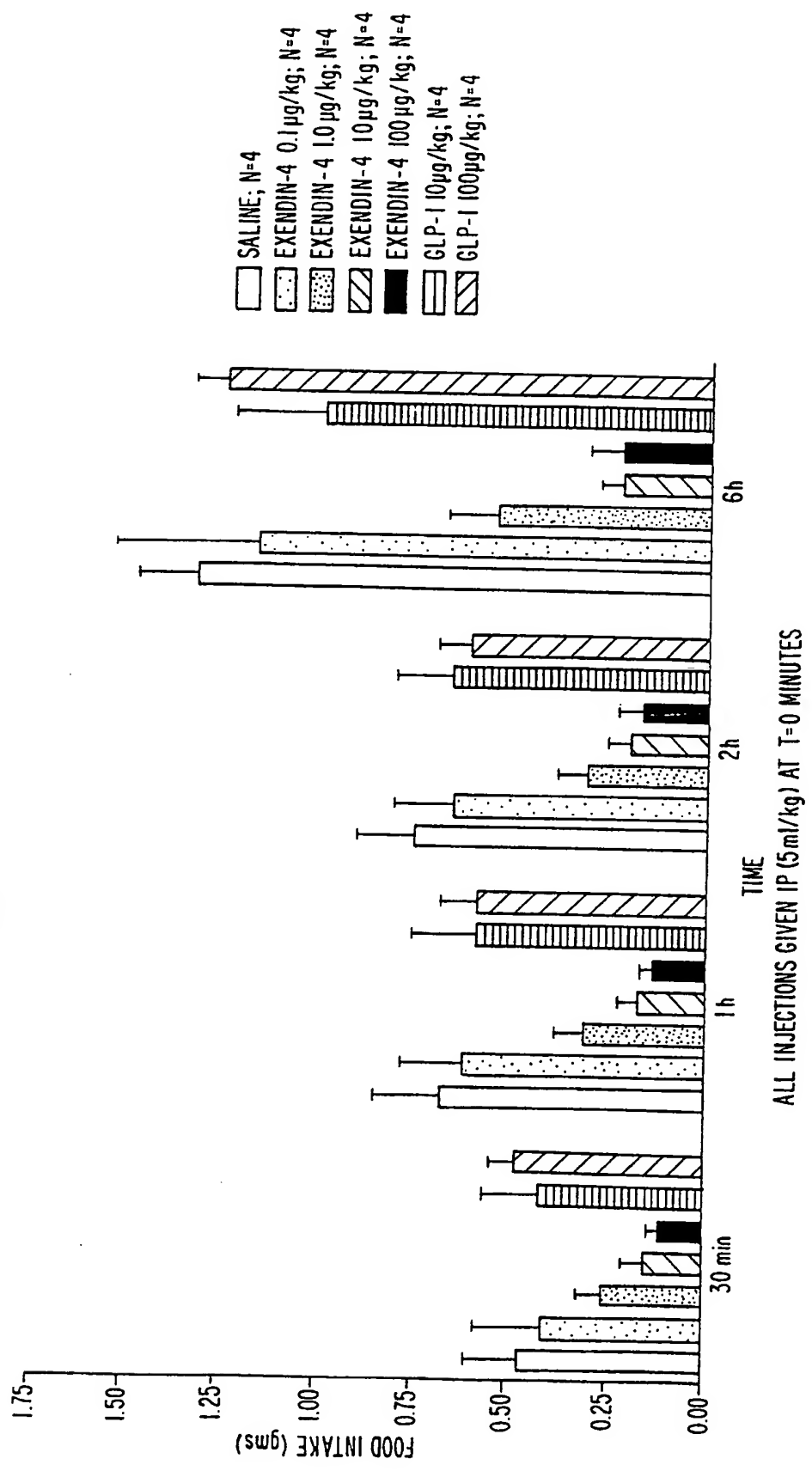

SALINE; N=4
EXENDIN-4 0.1µg/kg; N=4
EXENDIN-4 1.0µg/kg; N=4
EXENDIN-4 10µg/kg; N=4
EXENDIN-4 100µg/kg; N=4
GLP-1 10µg/kg; N=4
GLP-1 100µg/kg; N=4
FOOD INTAKE (gms)
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
30 min
1h
2h
6h
TIME
ALL INJECTIONS GIVEN IP (5ml/kg) AT T=0 MINUTES

FIG. 2.

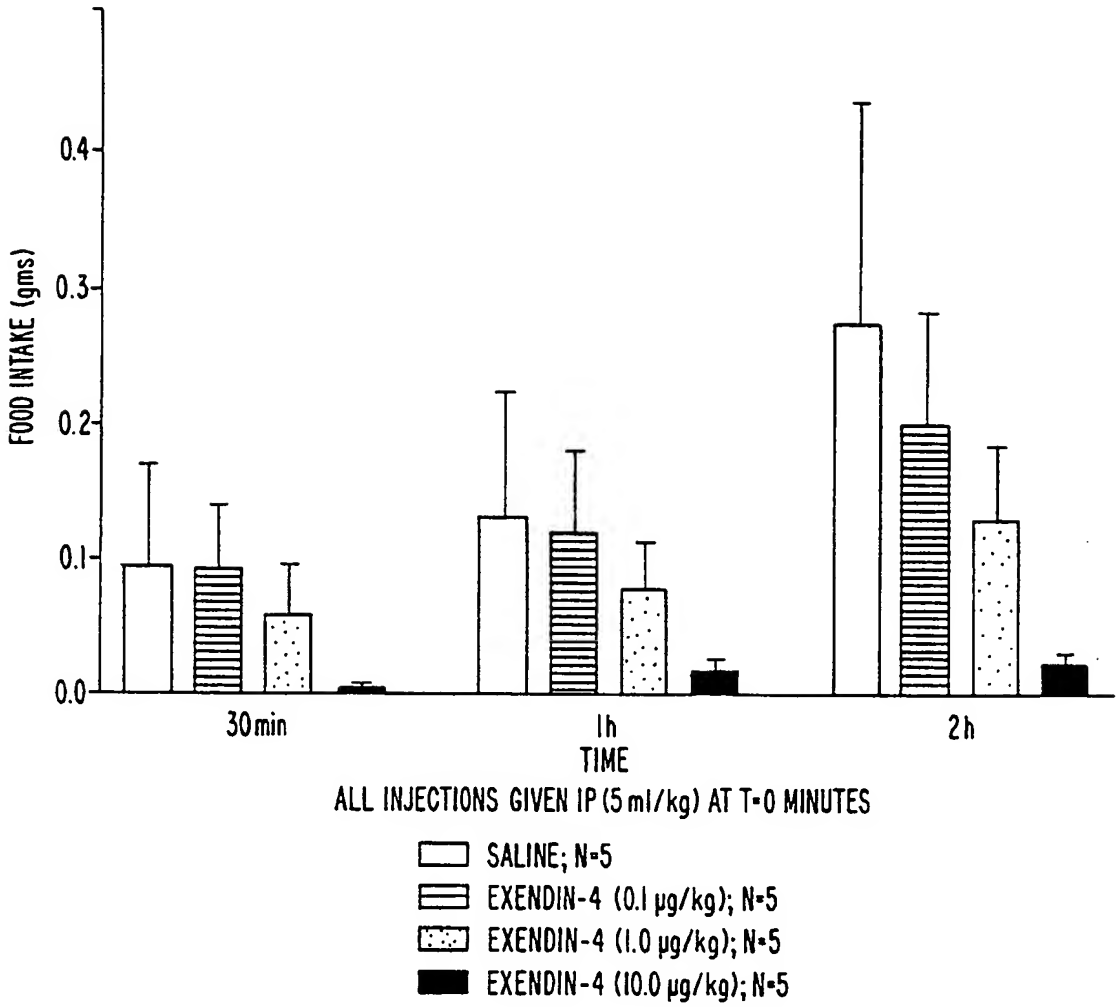
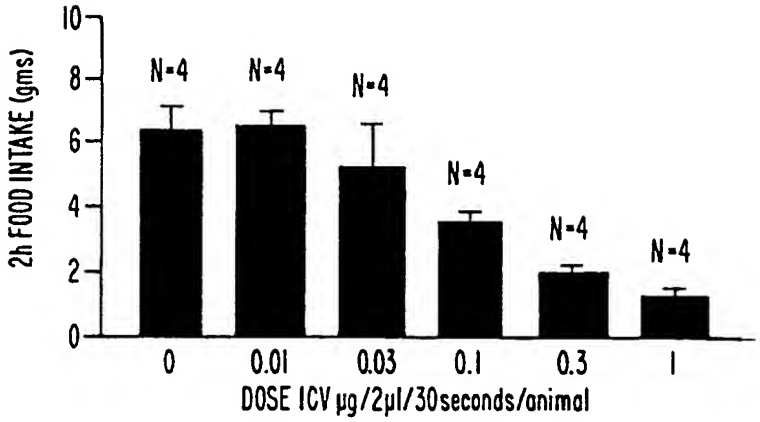
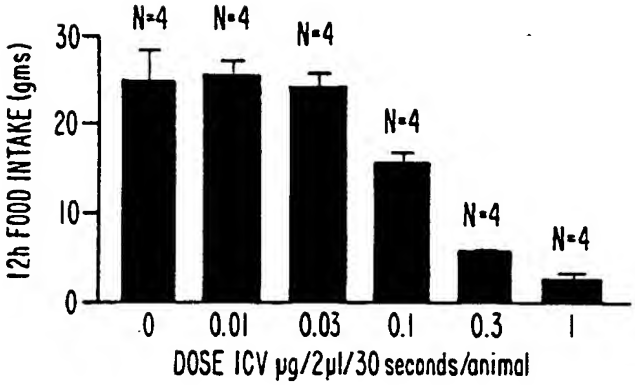

FOOD INTAKE (gms)
0.4
0.3
0.2
0.1
0.0
30 min
1h
2h
TIME
ALL INJECTIONS GIVEN IP (5 ml/kg) AT T=0 MINUTES
SALINE; N=5
EXENDIN-4 (0.1 µg/kg); N=5
EXENDIN-4 (1.0 µg/kg); N=5
EXENDIN-4 (10.0 µg/kg); N=5

FIG. 3.


2h FOOD INTAKE (gms)
10
8
6
4
2
0
N=4
N=4
N=4
N=4
N=4
N=4
0
0.01
0.03
0.1
0.3
1
DOSE ICV µg/2µl/30seconds/animal


12h FOOD INTAKE (gms)
30
20
10
0
N=4
N=4
N=4
N=4
N=4
N=4
0
0.01
0.03
0.1
0.3
1
DOSE ICV µg/2µl/30 seconds/animal

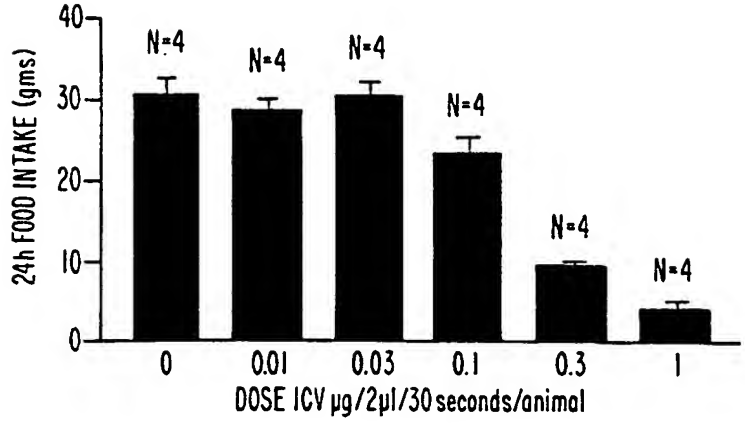

24h FOOD INTAKE (gms)
40
30
20
10
0
N=4
N=4
N=4
N=4
N=4
N=4
0
0.01
0.03
0.1
0.3
1
DOSE ICV µg/2µl/30 seconds/animal

FIG. 4.

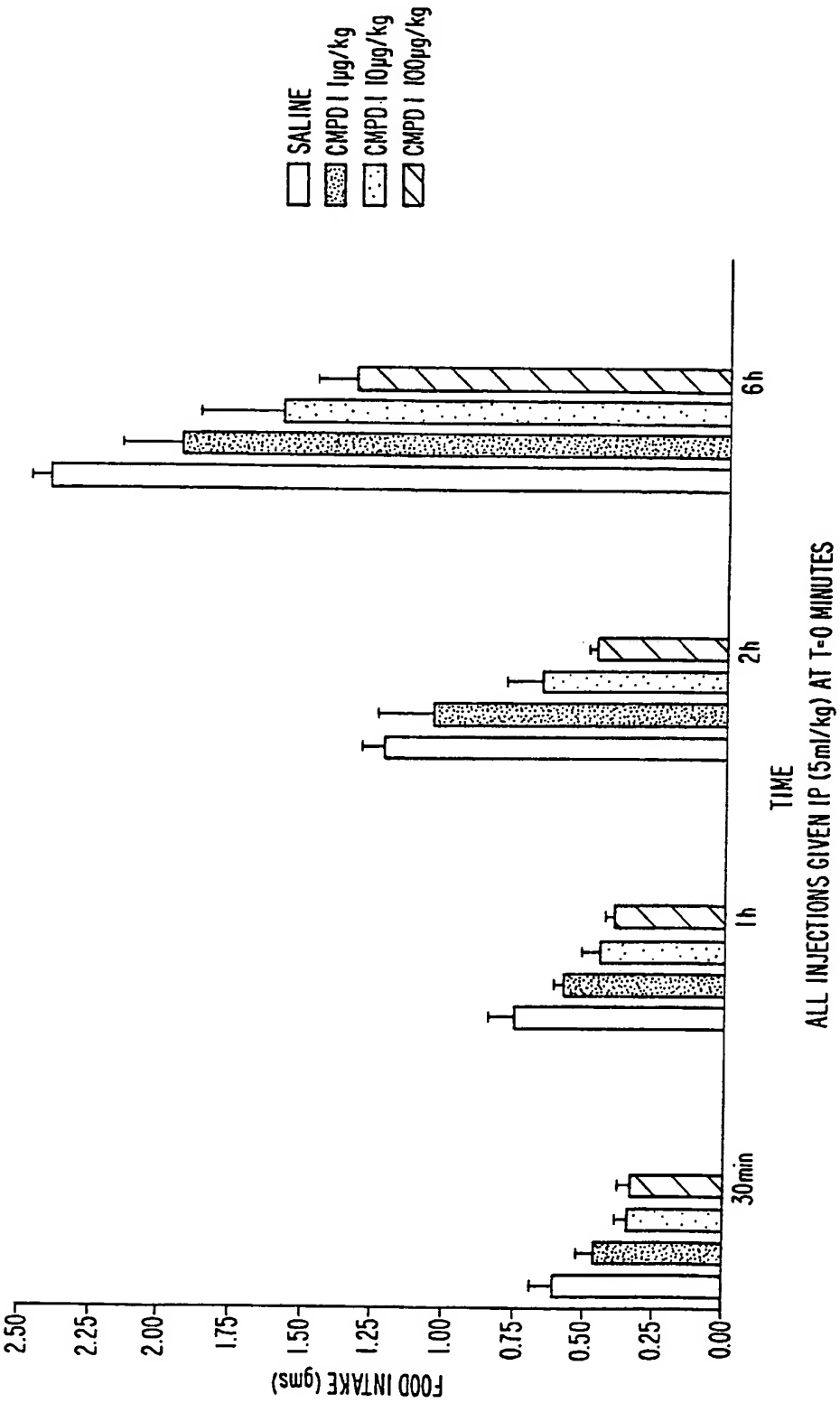

SALINE
CMPD I 1µg/kg
CMPD I 10µg/kg
CMPD I 100µg/kg
FOOD INTAKE (gms)
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
30min
1h
2h
6h
TIME
ALL INJECTIONS GIVEN IP (5ml/kg) AT T=0 MINUTES

FIG. 5.

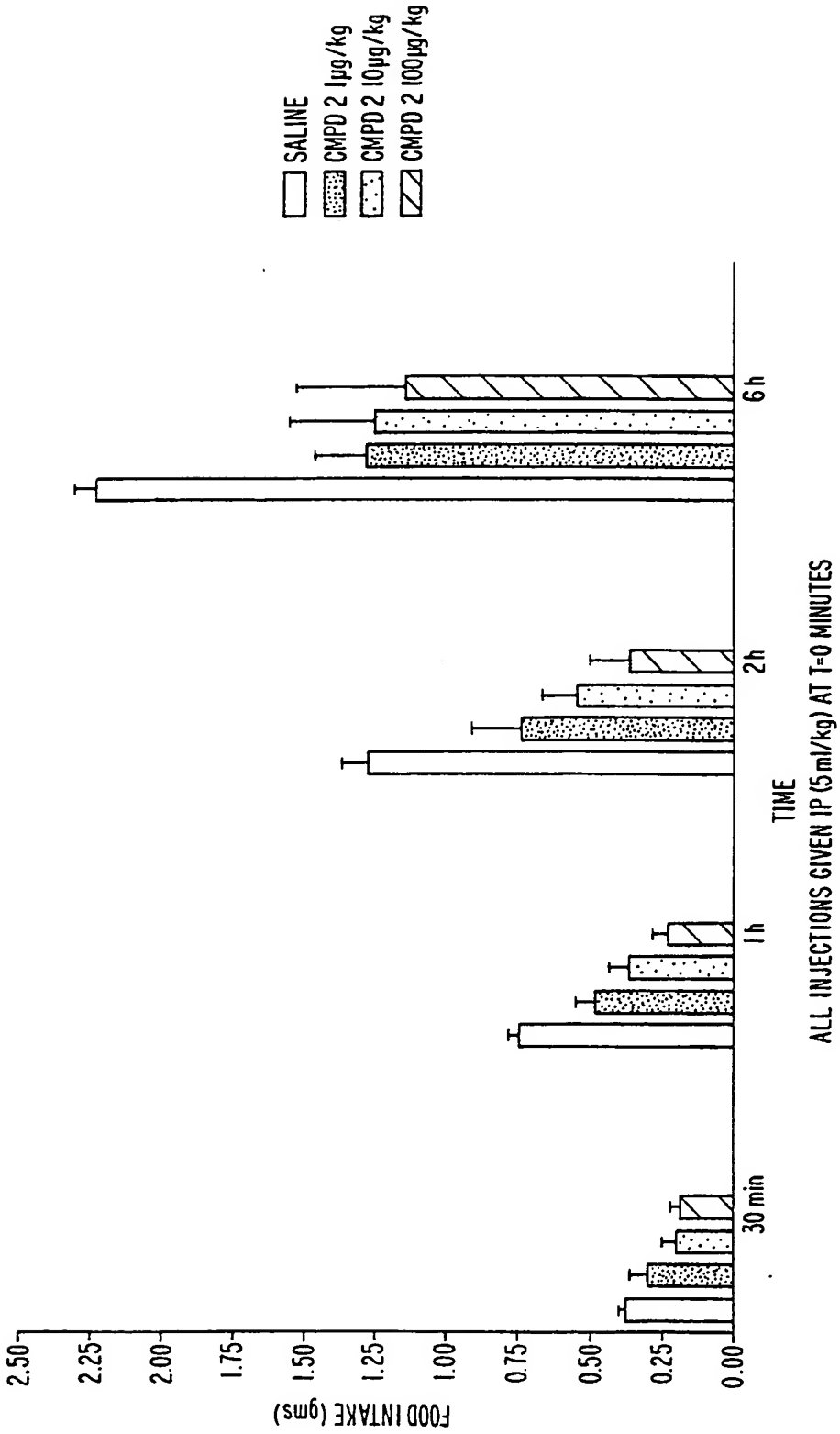

SALINE
CMPD 2 1µg/kg
CMPD 2 10µg/kg
CMPD 2 100µg/kg
FOOD INTAKE (gms)
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
30 min
1h
2h
6h
TIME
ALL INJECTIONS GIVEN IP (5ml/kg) AT T=0 MINUTES

FIG. 6.

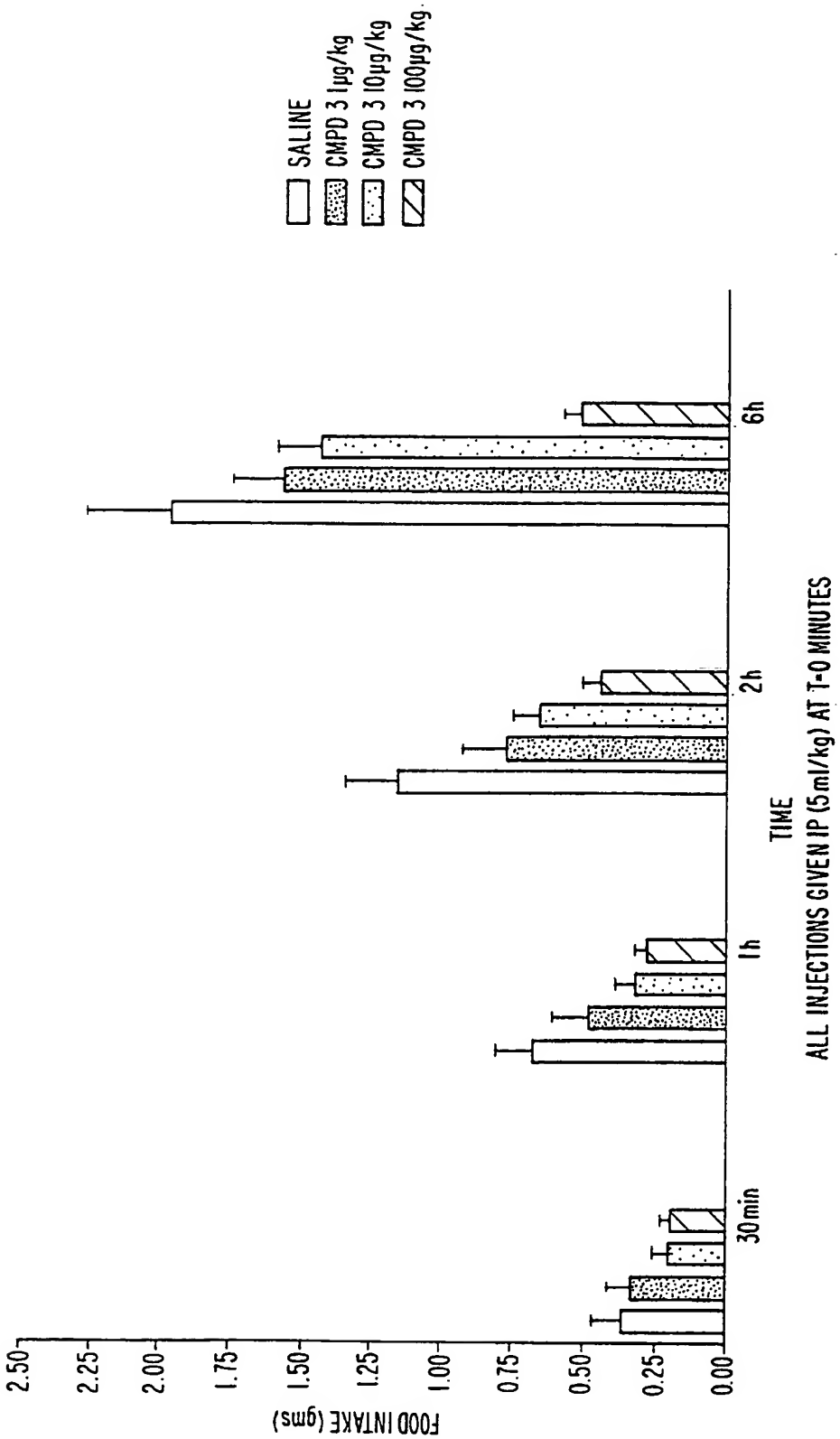

SALINE
CMPD 3 1µg/kg
CMPD 3 10µg/kg
CMPD 3 100µg/kg
FOOD INTAKE (gms)
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
30 min
1h
2h
6h
TIME
ALL INJECTIONS GIVEN IP (5 ml/kg) AT T=0 MINUTES

FIG. 7.

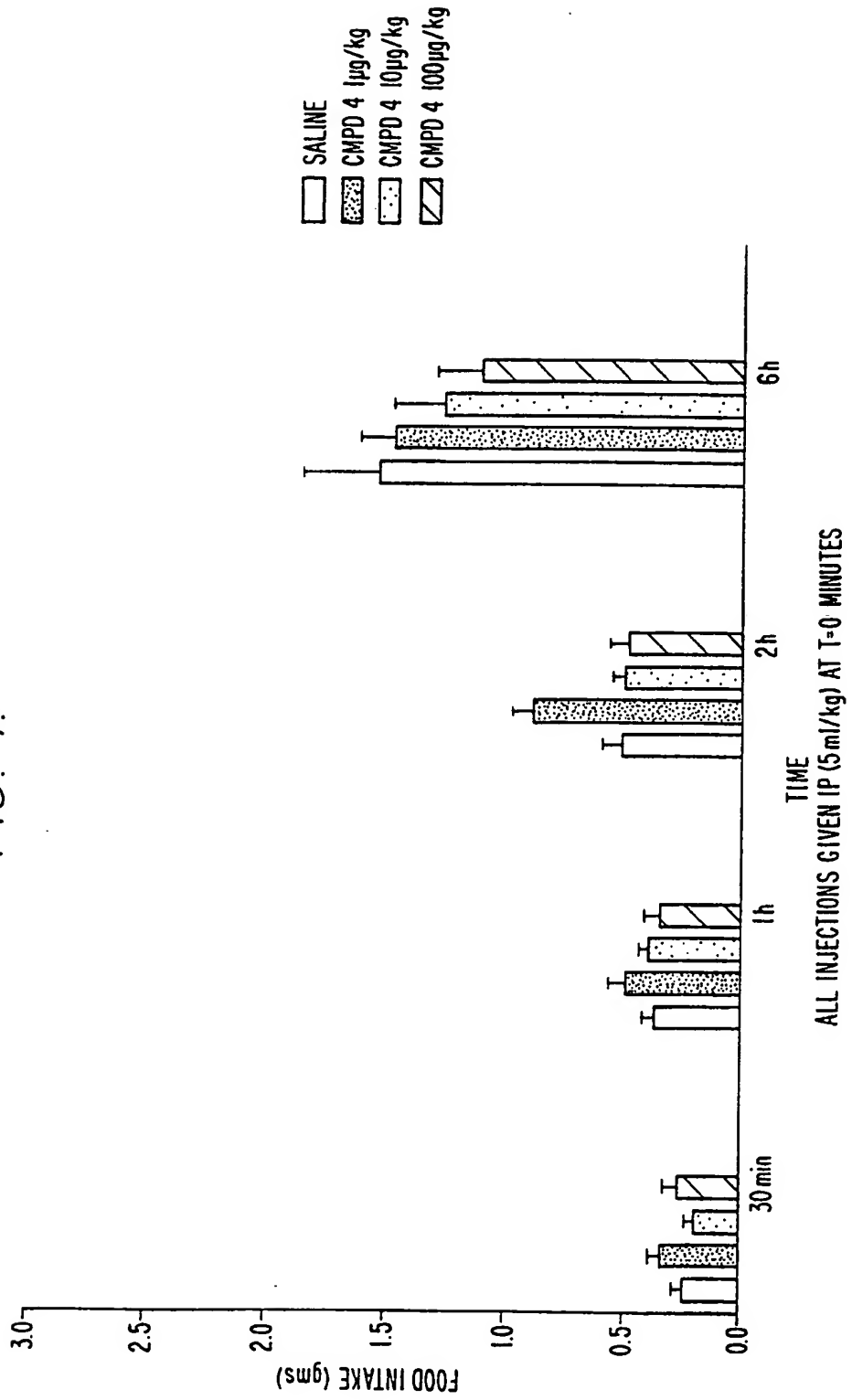

SALINE
CMPD 4 1µg/kg
CMPD 4 10µg/kg
CMPD 4 100µg/kg
FOOD INTAKE (gms)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
30 min
1h
2h
6h
TIME
ALL INJECTIONS GIVEN IP (5ml/kg) AT T=0 MINUTES

FIG. 8.

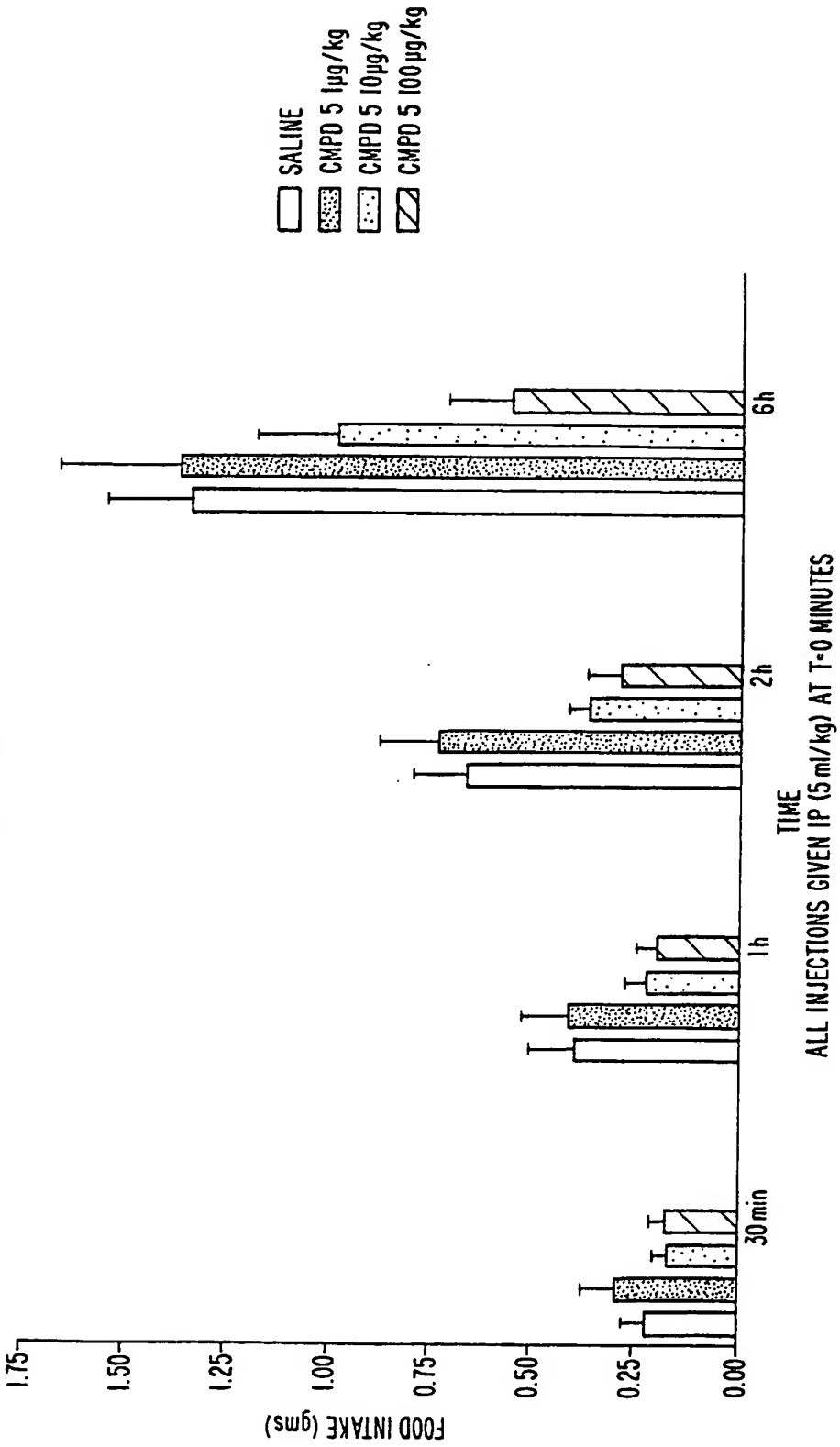
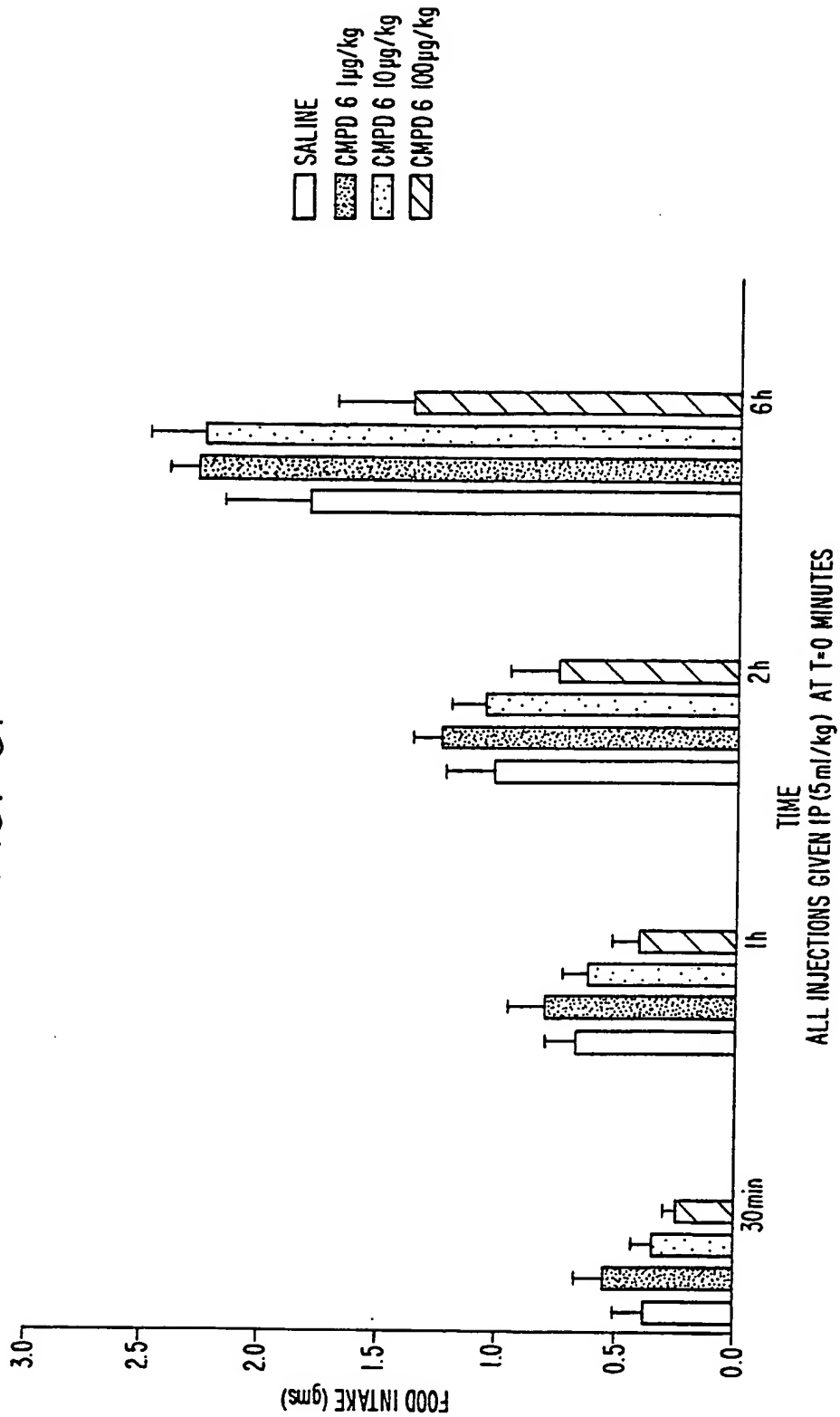

SALINE
CMPD 5 1µg/kg
CMPD 5 10µg/kg
CMPD 5 100µg/kg
FOOD INTAKE (gms)
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
30 min
1h
2h
6h
TIME
ALL INJECTIONS GIVEN IP (5ml/kg) AT T=0 MINUTES

FIG. 9.


SALINE
CMPD 6 1µg/kg
CMPD 6 10µg/kg
CMPD 6 100µg/kg
FOOD INTAKE (gms)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
30min
1h
2h
6h
TIME
ALL INJECTIONS GIVEN IP (5ml/kg) AT T=0 MINUTES

1 5 10 15 20
Xaa_1 Xaa_2 Xaa_3 Gly Thr Xaa_4 Xaa_5 Xaa_6 Xaa_7 Xaa_8 Ser Lys Gln Xaa_9 Glu Glu Glu Ala Val Arg Leu
25 30 35
Xaa_{10} Xaa_{11} Xaa_{12} Xaa_{13} Leu Lys Asn Gly Gly Xaa_{14} Ser Ser Gly Ala Xaa_{15} Xaa_{16} Xaa_{17} Xaa_{18}-Z

[SEQ. ID. NO.]	Xaa_1	Xaa_2	Xaa_3	Xaa_4	Xaa_5	Xaa_6	Xaa_7	Xaa_8	Xaa_9	Xaa_{10}	Xaa_{11}	Xaa_{12}	Xaa_{13}	Xaa_{14}	Xaa_{15}	Xaa_{16}	Xaa_{17}	Xaa_{18}	Z
9	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Leu	Phe	Ile	Glu	Phe	Pro	Pro	Pro	Pro	Ser	NH_2
10	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Leu	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
11	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Phe	Pro	Pro	Pro	Pro	Ser	NH_2
12	Tyr	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
13	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Tyr	NH_2
14	His	Gly	Asp	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
15	His	Gly	Glu	naph	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
16	His	Gly	Glu	Phe	Ser	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
17	His	Gly	Glu	Phe	Ser	Thr	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
18	His	Gly	Glu	Phe	Thr	Thr	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
19	His	Gly	Glu	Phe	Thr	Ser	Glu	Leu	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
20	His	Gly	Glu	Phe	Thr	Ser	Asp	pGly	Met	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
21	His	Gly	Glu	Phe	Thr	Ser	Asp	pGly	Leu	Phe	Ile	Glu	Phe	Pro	Pro	Pro	Pro	Ser	NH_2
22	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	pGly	Phe	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2

FIGURE 10
(Sheet 1 of 2)

[SEQ. ID. NO.]	Xaa_1	Xaa_2	Xaa_3	Xaa_4	Xaa_5	Xaa_6	Xaa_7	Xaa_8	Xaa_9	Xaa_{10}	Xaa_{11}	Xaa_{12}	Xaa_{13}	Xaa_{14}	Xaa_{15}	Xaa_{16}	Xaa_{17}	Xaa_{18}	Z
23	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	pGly	Phe	Ile	Glu	Phe	Pro	Pro	Pro	Pro	Ser	NH_2
24	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	naph	Ile	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
25	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Val	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
26	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Leu	Phe	Val	Glu	Phe	Pro	Pro	Pro	Pro	Ser	NH
27	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	tBuG	Glu	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
28	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Leu	Phe	tBuG	Glu	Phe	Pro	Pro	Pro	Pro	Ser	NH_2
29	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Asp	Trp	Pro	Pro	Pro	Pro	Ser	NH_2
30	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Phe	Pro	Pro	Pro	Pro	Ser	NH_2
31	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	tPro	tPro	tPro	tPro	Ser	NH_2
32	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	tPro	tPro	tPro	Ser	NH_2
33	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	hPro	hPro	hPro	hPro	Ser	NH_2
34	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	hPro	hPro	hPro	Ser	NH_2
35	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Leu	Phe	Ile	Glu	Phe	tPro	tPro	tPro	tPro	Ser	NH_2
36	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Leu	Phe	Ile	Glu	Phe	hPro	hPro	hPro	hPro	Ser	NH_2
37	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	MeAla	MeAla	MeAla	MeAla	Ser	NH
38	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Met	Phe	Ile	Glu	Trp	Pro	MeAla	MeAla	MeAla	Ser	NH_2
39	His	Gly	Glu	Phe	Thr	Ser	Asp	Leu	Leu	Phe	Ile	Glu	Phe	MeAla	MeAla	MeAla	MeAla	Ser	NH_2

FIGURE 10
(Sheet 2 of 2)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/00449

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61K 38/16
US CL : 514/2, 866
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 514/2, 866

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,424,286 A (ENG) 13 June 1995 see entire document.	1-31

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 07 MAY 1998	Date of mailing of the international search report 29 MAY 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Zohreh Fay Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet)(July 1992)*